EXHIBIT 1

IN THE UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF ARKANSAS
WESTERN DIVISION

In re:	:	MDL Docket No. 4:03CV1507-WRW 4:05CV00163
PREMPRO PRODUCTS LIABILITY LITIGATION	:	
LINDA REEVES	:	PLAINTIFF
v.	:	
WYETH	:	DEFENDANT

ORDER

Pending are Defendant's Motion to Exclude Expert Testimony of Dr. Fugh-Berman (Doc. No. 77), Motion to Exclude Expert Testimony of Dr. Bundred (Doc. No. 88), Motion to Exclude Expert Testimony of Dr. Colditz (Doc. No. 94), Defendant's Motion to Exclude Expert Testimony of Mr. Maloney (Doc. No. 96), and Motion to Compel the Production of Annotated Document Prepared by Plaintiff's Regulatory Expert, Dr. John Gueriguian (Doc. No. 124). Also pending is Plaintiff's Motion to Exclude the Testimony of Leon Speroff (Doc. No. 117).

Based on the findings of fact and conclusions of law, as well as statements of counsel, made at the hearings held on July 13-14, 2006, I rule as follows:

1. Defendant's Motion to Exclude Expert Testimony of Dr. Fugh-Berman (Doc. No. 77) is DENIED AS MOOT.

2. Defendant's Motion to Exclude Expert Testimony of Dr. Bundred (Doc. No. 88) is DENIED AS MOOT.

3. Defendant's Motion to Compel the Production of Annotated Document Prepared by Plaintiff's Regulatory Expert, Dr. John Gueriguian (Doc. No. 124) is DENIED AS MOOT.

4. Defendant's Motion to Exclude Expert Testimony of Dr. Colditz (Doc. No. 94) is DENIED. However, Dr. Colditz's testimony will be limited to general causation and identifying the resources available to make the risk/benefit analysis of HRT. At this point, Dr. Colditz will not be permitted to testify that the risks of HRT outweigh the benefits.

5. Defendant's Motion to Exclude Expert Testimony of Mr. Maloney (Doc. No. 96) is DENIED AS MOOT. As I recall, the necessity for this witness is obviated by the $12 billion net worth stipulation.

6. Plaintiff's Motion to Exclude the Testimony of Leon Speroff (Doc. No. 117) is GRANTED IN PART and DENIED IN PART. To the extent that Plaintiff requests that Defendant be precluded from referring to Dr. Speroff's deposition testimony at trial, the motion is DENIED. To the extent that Plaintiff requests to conduct a supplemental deposition of Dr. Speroff, the motion is GRANTED.

7. As was discussed at the July 14, 2006 hearing, this case is CONTINUED. Accordingly, the trial will commence at 9 a.m., Monday, August 21, 2006.

IT IS SO ORDERED this18th day of July, 2006.

/s/ Wm. R. Wilson, Jr.
UNITED STATES DISTRICT JUDGE

EXHIBIT 2

IN THE UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF ARKANSAS
WESTERN DIVISION

In re:	:	MDL Docket No. 4:03CV1507-WRW
	:	4:05CV00497
PREMPRO PRODUCTS LIABILITY LITIGATION	:	
	:	
	:	
HELENE RUSH	:	PLAINTIFF
	:	
v.	:	
	:	
WYETH	:	DEFENDANT

ORDER

Pending are several *Daubert* motions: Defendant's Motion to Exclude Expert Testimony of Drs. Klimberg and Waldron as to Specific Causation (Doc. No. 136); Defendant's Motion to Exclude Expert Testimony of Dr. Hollon (Doc. No. 140); Defendant's Motion to Exclude Testimony of Dr. Gueriguian (Doc. No. 142); Defendant's Motion to Exclude Expert Testimony of Dr. Sackett (Doc. No. 144); and Defendant's Motion to Exclude Expert Testimony of Dr. Austin (Doc. No. 148).[1] Also pending are Plaintiff's Motion to Preclude Defendant's Experts from Testifying That There is No Reliable Scientific Evidence that Combination Hormone Therapy Can Cause Breast Cancer (Doc. No. 193)[2] and Defendant's Motion for Summary Judgment Re: Specific Causation (Doc. No. 87).[3] Oral argument was heard on July 13-14, 2006 and again on July 31, 2006.

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[1]Plaintiff has responded to each motion (Doc. Nos. 211, 215, 213, 203).

[2]Defendant has responded (Doc. No. 225).

[3]Plaintiff has responded (Doc. No. 111) and Defendant has replied (Doc. No. 175).

I. STANDARD

A. Burden of Proof

The admission of expert testimony is governed by Rule 702 of the Federal Rules of Evidence, which reads:

> If scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue a witness qualified as an expert by knowledge, skill, experience, training, or education, may testify thereto in the form of an opinion or otherwise, if (1) the testimony is based upon sufficient facts or data, (2) the testimony is the product of reliable principles and methods, and (3) the witness has applied the principles and methods reliably to the facts of the case.[4]

When a party proffers an expert witness, deciding whether Rule 702 is satisfied is a preliminary issue governed by Federal Rule of Evidence 104(a).[5] Rule 104(a) requires the proponent of evidence to establish its admissibility by a preponderance of the evidence.[6] In determining admissibility, the court is not bound by any of the rules of evidence, except with regard to privilege.[7]

B. Legal Standard for Admissibility

The central inquiry under Rule 702 is whether the proffered expert's testimony is sufficiently reliable.[8] The trial court serves a gatekeeping function, ensuring that any expert testimony is reliable and relevant.[9]

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[4] Fed. R. Evid. 702.

[5] *U.S. v. Martinez*, 3 F.3d 1191, 1196 n.10 (8th Cir. 1993).

[6] *Bourjaily v. U.S.*, 483 U.S. 171 (1987).

[7] Fed. R. Evid. 104(a).

[8] *First Nat'l Bank v. Benham*, 423 F.3d 855, 861 (8th Cir. 2005).

[9] *Id.*

To be admissible, expert testimony must satisfy the two prongs of Rule 702.[10] First, it must be based on scientific, technical, or other specialized knowledge.[11] If the testimony is scientific, it must be grounded in the methods and procedures of science.[12] Likewise, "knowledge" requires more than a subjective belief or an unsupported speculation, requiring instead an appropriate level of validation.[13] Second, the testimony must be relevant, in that it must help the trier of fact either understand the evidence or determine a fact in issue.[14] The burden of establishing relevancy and reliability rests on the proponent of the expert testimony.[15]

Courts have used a variety of factors to determine the reliability of proffered expert testimony. The most frequently discussed factors are those derived from the Supreme Court's opinion in *Daubert*, where the Court established that the trial court may consider:

> (1) whether the theory or technique can be or has been tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether the theory or technique has a known or potential error rate and standards controlling the technique's operation; and (4) whether the theory or technique is generally accepted in the scientific community.[16]

Because the inquiry is "flexible and fact-specific, a court should use, adapt, or reject *Daubert* factors" as needed based on the facts of a particular case.[17]

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[10] *U.S. v. Cawthorn*, 429 F.3d 793, 799 (8th Cir. 2005).

[11] *Id.*

[12] *Id.*

[13] *Id.* at 799-800 (*quoting Daubert v. Merrell Dow Pharms.*, 509 U.S. 579, 590 (1993)).

[14] *Id.* at 799.

[15] *Moore v. Ashland Chem., Inc.*, 151 F.3d 269, 278-78 (5th Cir. 1998).

[16] *Benham*, 423 F.3d at 861 (*citing Daubert*, 509 U.S. at 593-94).

[17] *Unrein v. Timesavers, Inc.*, 394 F.3d 1008, 1011 (8th Cir. 2005).

The most recent amendments to Rule 702 added three general standards for courts to use in determining the reliability and relevance of proffered expert testimony. First, the proffered testimony must be based on sufficient facts or data.[18] Second, it must be the product of reliable principles and methods.[19] Third, the expert must have applied those principles and methods reliably to the facts of the case.[20]

The focus is not on the expert's conclusion, but on the methodology.[21] The proponent of the testimony "need not prove . . . that the expert's testimony is correct, but . . . must prove by a preponderance of the evidence that the testimony is reliable."[22] Determining the validity of an expert's conclusions is the duty of the finder of fact.

II. ANALYSIS

A. Defendant's Motion to Exclude Expert Testimony of Drs. Klimberg and Waldron as to Specific Causation (Doc. No. 136)

Drs. Suzanne Klimberg and James A. Waldron were retained by Plaintiff to testify on both the general and specific causation of Plaintiff's breast cancer.

Defendant asserts several reasons for excluding the expert testimony of Drs. Klimberg and Waldron: (1) the opinions were created exclusively for this litigation; (2) the opinions are not based on sufficient facts or data;[23] (3) differential diagnosis is not reliable to determine the

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[18]Fed. R. Evid. 702(1).

[19]Fed. R. Evid. 702(2).

[20]Fed. R. Evid. 702(3).

[21]*Moore*, 151 F.3d at 275-76.

[22]*Id* at 276.

[23]Specifically Defendant claims that the opinions lack support because: (1) scientists do not know what causes breast cancer in an individual woman; (2) there is no test to identify the

cause of breast cancer; (4) and the "Gail Model" is not reliable to determine the cause of breast cancer.[24] Defendant also contends that Drs. Klimberg and Waldron are not qualified to testify because Dr. Klimberg has "never published -- or even presented -- the opinions regarding the cause of breast cancer" and Dr. Waldron's "previous experience with breast cancer was limited to analyzing breast biopsies and determining whether the tissue was cancerous, not identifying the cause of cancer."[25]

Plaintiff counters that Drs. Klimberg's and Waldron's opinions are based on scientifically reliable evidence. Additionally, Plaintiff claims that as a surgical oncologist and director of the breast cancer program at the Arkansas Cancer Research Center at UAMS[26] (Dr. Klimberg) and a diagnostic surgical pathologist and professor of pathology at UAMS (Dr. Waldron), both experts are qualified to testify as experts regarding causation.

Defendant's attacks on Drs. Klimberg's and Waldron's qualifications do not pass muster. Both experts have experience and understanding regarding breast cancer and their opinions are bottomed upon scientifically reliable information.

In formulating their opinions, Drs. Klimberg and Waldron relied on their training, knowledge, and experience as a surgical oncologist and pathologist, respectively. They reviewed and relied on numerous published, peer-reviewed medical literature and studies. While

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cause of breast cancer; (3) there is no physical characteristic that distinguishes breast cancers based on their cause; and (4) there is no way to separate the effect of naturally-occurring hormones and hormone therapy. *See* Doc. No. 137.

[24]Doc. No. 137.

[25]Doc. No. 137.

[26]University of Arkansas for Medical Sciences.

both reports are primarily conclusive, rather than explanatory, I don't believe that either expert used improper methodology. Dr. Klimberg's report on general causation reads:

> To make a causal assessment in an individual case, one would need to consider the totality of evidence, including statistical association, details about generally recognized and statistically significant risk factors, physiological response to the drugs, such as radiological evidence of changes in breast density before, during, and after hormone therapy use, pathological biomarkers in the breast tissue samples during biopsy and surgery, as well as duration of use of the hormone therapy drugs.[27]

Defendant faults the experts for using differential analysis. However, reliance on differential analysis is not fatal when epidemiological studies also support the expert's conclusions.[28] Raising significant questions about the experts' analysis and conclusions is something Defendant can do for the jury.

Also, Defendant claims that, since scientists don't know what causes breast cancer, Plaintiff's experts cannot opine that Plaintiff's breast cancer was caused by HRT. Defendant's focus is too narrow. Plaintiff's experts need not conclude that HRT definitively caused Plaintiff's cancer; they must only establish that it was more likely than not a cause -- or that it promoted her cancer. That said, Plaintiff's experts' conclusions that HRT was "a substantial contributing factor"[29] in the development or promotion of Plaintiff's breast cancer chins the pole.

Again, while both reports are somewhat conclusive, rather than explanatory, I cannot say that either expert used improper methodology. In sum, both experts are qualified to testify that

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[27]Doc. No. 157, Ex. 20.

[28]*See Ambrosini v. Labarraque*, 101 F.3d 129, 140-41 (D.C. Cir. 1996) (holding that expert testimony which relied, in part, on a differential analysis ruling out alternative sources of plaintiff's injury, was admissible, where epidemiological studies also indicated causal nexus).

[29]Doc. No. 157, Exs. 21, 29.

HRT more likely than not caused or promoted Plaintiff's breast cancer. Their conclusions can be tested during cross-examination.

B. Defendant's Motion to Exclude the Expert Testimony of Dr. Austin (Doc. No. 148)

Dr. Donald Austin will testify that, with proper monitoring, Wyeth could have and should have detected a signal in the 1980s that HRT may have been causing a disproportionate increase in certain types of breast cancer. Dr. Austin focused his report on "whether routine monitoring of breast cancer incidence from a publicly available source of such data of [sic] could have identified an anomalous increase in the incidence of invasive lobular carcinoma ["ILC"] in the U.S. during the period 1980-2000."[30]

Defendant contends that Dr. Austin's expert testimony should be excluded because: (1) it is unreliable since it was "developed solely for litigation," has not been tested, and has not been peer-reviewed or published;[31] (2) it does not "fit"[32] in the facts of this case because Ms. Rush did not have ILC; (3) none of Dr. Austin's findings can be used as evidence that HRT increased the risk of breast cancer of any type; and (4) there is no evidence that information about increased risk of particular breast cancer cell types would have affected a physician's decisions to prescribe HRT.[33]

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[30]Doc. No. 157, Ex. 1.

[31]Doc. No. 149.

[32]*See Concord Boat Corp. v. Brunswick Corp.*, 207 F.3d 1039, 1055 (8th Cir. 2000) (recognizing that "[i]n recent years the Supreme Court has put renewed emphasis on the importance of the 'fit' of an expert's opinion to the data or facts in the case").

[33]Doc. No. 149.

1. Unreliable -- Wyeth's arguments on this point are standard *Daubert* challenges. However, these challenges are insufficient, even when considered cumulatively. First, "the fact of publication (or lack thereof) in a peer reviewed journal [is] . . . a relevant, though not dispositive, consideration."[34] Second, the fact that this research was conducted solely for this litigation, while noteworthy, is not fatal. When an expert develops opinions "expressly for the purposes of testifying," the proponent is required to "come forward with other objective, verifiable evidence that the testimony is based on 'scientifically valid principles.'"[35] Here, Dr. Austin's objective evidence is the SEER database he reviewed when compiling the data regarding the number of breast cancer incidences. As far as I can tell, Dr. Austin researched the database looking for a trend and reported the information that he discovered. Additionally, I don't find anything scientifically infirm about compiling data. It appears to me that the conclusions he makes are based on a review of the objective evidence in the database.

2. "Fit"-- Defendant also contends that Dr. Austin's findings are not relevant to this case because Plaintiff was diagnosed with ductal breast cancer, and Dr. Austin's findings refer to lobular breast cancer. Specifically, Dr. Austin concludes that his findings "represent a real and statistically significant increase in the proportions of ILC and Mixed Ductal/Lobular cancer relative to all invasive breast carcinoma."[36] Relying on Dr. Austin's report, Plaintiff contends that had Wyeth been keeping track of the information in the SEER database, it would have noticed "a surge in lobular breast cancer that mirrored the rise in the sale of E+P."[37]

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[34] *Daubert*, 509 U.S. at 593.

[35] *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 43 F.3d 1311, 1317-18 (9th Cir. 1995) (*quoting Daubert*, 509 U.S. at 597).

[36] Doc. No. 157, Ex. 2.

[37] *Reeves v. Wyeth*, 4:05-CV-00163 (E.D. Ark.), Doc. No. 266.

Plaintiff further contends that this "knowledge would have caused a reasonably prudent manufacturer to conduct further studies on all hormone positive breast cancers," probably resulting in the issuance of an adequate label before Plaintiff's ductal cancer was caused or promoted.[38]

While I have some doubt about Dr. Austin's analysis, "doubts regarding whether an expert's testimony will be useful should generally be resolved in favor of admissibility."[39]

3. Causation -- Plaintiff and Dr. Austin both concede that he could not comment on causation.[40] Accordingly, Dr. Austin will not be permitted to testify regarding causation.

4. Irrelevant to Prescribing Decision -- Defendant also contends that Dr. Austin's testimony is irrelevant because "there is no evidence that information about risk of particular breast cancer cell types -- as opposed to the overall risk of breast cancer -- would matter to doctors in prescribing hormone therapy."[41] Since Plaintiff is presenting Dr. Austin's testimony to establish "what *defendants* should have done with the information, not what physicians would have done,"[42] Defendant is off the mark. Plaintiff's position is well-taken.

C. Defendant's Motion to Exclude the Expert Testimony of Dr. Hollon (Doc. No. 140).

Dr. Matthew Hollon plans to testify that Wyeth failed to meet the reasonable standard for care for drug promotion. He contends that Wyeth used promotional techniques irresponsibly and

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[38] *Id.*

[39] *Clark by and through Clark v. Heidrick*, 150 F.3d 912, 915 (8th Cir. 1998).

[40] Doc. No. 157, Ex. 1 and Doc. No. 285.

[41] Doc. No. 232.

[42] Doc. No. 203 (emphasis in original).

excessively, which directly influence physicians' prescribing practices.[43] Plaintiff asserts that Dr. Hollon should be permitted to testify that "Wyeth engaged in longstanding manipulation of conventional wisdom on hormone therapy . . . [and] that physicians are influenced by marketing, notwithstanding their denials."[44]

Dr. Hollon is a practicing physician in internal medicine, with a Masters in Public Health, who has published several articles on pharmaceutical advertising.[45] He also teaches at the University of Washington in Seattle, and "has conducted independent social science research and written evidenced-based reviews and editorials" on pharmaceutical marketing.[46]

Defendant points out that although Dr. Hollon has published several pieces on pharmaceutical advertising, they were all editorials.[47] As stated above, Wyeth contends that Dr. Hollon should be prevented from testifying because his positions are not scientific, but personal opinions. Dr. Hollon's testimony need not be scientific. Rule 702 permits a witness to testify in the form of an opinion when that expert possesses scientific, technical, or other specialized knowledge that will assist the trier of fact. Clearly, Dr. Hollon has a knowledge of pharmaceutical marketing that is beyond a juror's common understanding. Although Defendant challenges the basis for his opinions, such challenges are issues for cross-examination.

However, Dr. Hollon's testimony about Wyeth's marketing will be limited to the issues in this case. For example, Plaintiff's position that "Dr. Hollon's expertise transcends the

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[43]Doc. No. 157, Ex. 16.

[44]Doc. No. 209.

[45]Doc. No. 157, Ex. 16.

[46]Doc. No. 209.

[47]*Reeves v. Wyeth*, 4:05-CV-00163 (E.D. Ark.), July 31, 2006, Tr. at 141-142.

individual transaction to examine the general influence of promotional activities that violate public health principles" and "that given the extent of the promotional campaign, [Wyeth] certainly had undue influence on prescribing practices within this country" is too broad.[48] The United States Supreme Court has held that, even at the punitive damages stage of a trial, evidence of tortious conduct "must have a nexus to the specific harm suffered by the plaintiff . . . A defendant should be punished for the conduct that harmed the plaintiff, not for being an unsavory individual or business."[49]

It seems to me that any evidence of Defendant's "badness" during the punitive damage portion of the trial (if there is one) must be connected to Ms. Rush's injury. However, the nexus between Plaintiff and the advertisements need not be as strong as the causation requirements during the liability stage of the trial.[50] Dr. Hollon can testify regarding advertisements -- however, those advertisements must pertain to issues that are directly linked to Plaintiff, e.g. cardiac benefit, breast cancer, etc. Dr. Hollon will not be permitted to testify regarding general badness or badness in the specific areas which is not connected to Ms. Rush's injury.

D. Defendant's Motion to Exclude the Expert Testimony of Dr. John Gueriguian (Doc. No. 142)

In a July 24, 2006 letter, I requested that Plaintiff submit, as she suggested in the July 13-14, 2006 hearing, a short summary of Dr. Gueriguian's testimony.[51] In her July 27,

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[48]Doc. No. 141.

[49]*State Farm Mutual Auto. Ins. Co. v. Campbell*, 538 U.S. 408, 422-23 (2003).

[50]I previously held that Plaintiff would not be permitted to discuss advertisements that neither she nor her physician saw. However, at the punitive damages stage, the "nexus" can be a bit more attenuated.

[51]*Reeves v. Wyeth*, 4:05-CV-00163 (E.D. Ark.), Doc. No. 280.

2006 response letter, Plaintiff asserted that Dr. Gueriguian would present testimony regarding: (1) the United States Food and Drug Administration's ("FDA") role and authority; (2) the use and purpose of labels/warnings in communicating risk information to physicians and patients; (3) the history of Wyeth's HRT drugs; (4) breast cancer signals and Wyeth's failure to test for a connection between breast cancer and HRT; (5) purported cardiac and cognitive benefits of HRT and Wyeth's failure to test for such benefits; (6) assessment of the risks and benefits of a prescription drug; and (7) the differences between "estrogen alone, Old E+P, and New Prempro."[52] In sum, Dr. Gueriguian will testify about the history of the development of HRT and that Wyeth had a duty to WHI-type randomized controlled trial in 1980s, because that is what a reasonably prudent pharmaceutical company would do.[53]

Wyeth contends that Dr. Gueriguian's testimony should be excluded because: (1) his opinions will not assist the jury; (2) he lacks expertise to testify about Wyeth's marketing practices or FDA's review of promotional pieces; (3) he knows nothing about this specific case; and (4) he does not employ a reliable methodology.[54]

Dr. Gueriguian is a physician with specialty training in internal medicine, endocrinology, and pharmacology.[55] From 1978 to 1998 he worked at the FDA in the Division of Endocrine and Metabolic Drug Products. While at the FDA, Dr. Gueriguian reviewed drugs for safety and

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[52] *Reeves v. Wyeth*, 4:05-CV-00163 (E.D. Ark.), Doc. No. 289. *See also* Doc. No. 215.

[53] *Reeves v. Wyeth*, 4:05-CV-00163 (E.D. Ark.), July 13, 2006, Tr. at 130.

[54] Doc. No. 143.

[55] Doc. No. 215.

efficacy; applied FDA regulations regarding labeling, post-marketing surveillance, and approval of drugs; and was involved in the drafting of those regulations.[56]

1. FDA -- Plaintiff's assertion that "Wyeth has specifically stated that it has no challenge to this testimony"[57] appears to be premature if I correctly read paragraph 1 of Defendant's response letter of July 28, 2006.[58] I hold, in general, that Dr. Gueriguian's testimony on the points in the letter regarding the FDA are admissible.[59] I reserve the right, of course, to exclude specific testimony at the trial. This means that Plaintiff must pare Dr. Gueriguian's testimony on this point, as well as others, to the essentials.

2. Label/Warnings -- I will permit Dr. Gueriguian to relate a brief history (assuming it is based upon adequate data). Distilling voluminous documents is proper. While it is true that jurors can read documents, the trial would last months if they were required to read every admissible document. Further, I will permit Dr. Gueriguian to testify how he thinks Wyeth should have responded, but not how they would have.

3. History of Premarin and Prempro -- a short history will be permitted. See the next preceding paragraph.

4. Breast Cancer Signals -- Dr. Gueriguian will be permitted to testify that the recognition of signals should (not would) have led to studies and different warnings.

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[56] *Id.*

[57] *Reeves v. Wyeth*, 4:05-CV-00163 (E.D. Ark.), Doc. No. 289.

[58] *Reeves v. Wyeth*, 4:05-CV-00163 (E.D. Ark.), Doc. No. 297.

[59] *See In re Diet Drugs*, 2001 WL 454586, *24 (E.D. Pa. Feb. 1, 2001) (holding that "(a) Dr. Gueriguian's expert testimony about the standard of care in the pharmaceutical industry regarding the manner in which certain information should be communicated to the FDA; and (b) what FDA officials would have done with certain additional information such as particular adverse event reports" was admissible).

5. Cardiac Benefits -- Since Ms. Reeves was prescribed HRT based on the alleged cardiac benefit, Dr. Gueriguian's testimony regarding this issue is relevant.

6. Risk vs. Benefit -- this will be permitted, in general. In other words, he can testify about the risk/benefit considerations with respect to prescription drugs in general as well as this particular drug.

7. "New Prempro" -- After reading Plaintiff's Supplemental Filing Re: Wyeth's Motion in Limine No. 16 to Exclude Reference to "Low Dose" Prempro[60] and considering argument heard during the August 15, 2006 hearing, I believe Dr. Gueriguian should be permitted to refer to "Low-Dose" Prempro. (Since the drafting of this order, Defendant has filed a new motion regarding "Low-Dose" Prempro. This motion will be dealt with later today or tomorrow.)

Incidentally, I note that in paragraph 7 of Defendant's letter of July 28 (re: The Scope of Dr. Gueriguian's Testimony) states, "that is why this is a failure to warn, not a design defect case." I realize that this is Wyeth's position, but I have previously ruled that it is a design defect case too.

8. Reasonable Drug Company -- The last paragraph of Defendant's letter refers to Dr. Gueriguian's proposed testimony about "a reasonable drug company." Arkansas Code Annotated § 16-116-104 provides:

> (a)(1) In determining the liability of the manufacturer, the state of scientific and technological knowledge available to the manufacturer or supplier at the time the product was placed on the market, rather than at the time of the injury, may be considered as evidence.

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[60] *Reeves v. Wyeth*, 4:05-CV-00163 (E.D. Ark.), Doc. No. 291.

> (2) Consideration may also be given to the customary designs, methods, standards, and techniques of manufacturing, inspecting, and testing by other manufacturers or sellers of similar products.[61]

So, if Dr. Gueriguian has sufficient information, he can testify about the customs in the drug manufacturing world.

E. Defendant's Motion to Exclude the Expert Testimony of Dr. David Sackett (Doc. No. 144)

Dr. Sackett is prepared to testify that (1) Wyeth violated the principles of evidence-based medicine by failing to conduct a WHI-type study in the 1970s, and (2) that Wyeth intended to promote HRT for its potential cardiac benefits. Plaintiff contends that Dr. Sackett's testimony supports her negligence claim.[62]

Defendant contends that Dr. Sackett's testimony regarding the duty to perform a large, randomized study will be duplicative of Dr. Gueriguian's testimony. Defendant asserts that Dr. Sackett can't say what kind of study Wyeth should have conducted, and he doesn't follow a methodology, rely on any regulatory requirements, nor does he rely on any industry standards.[63]

Dr. Sackett is "a 40-year-veteran in the fields of internal medicine and clinical epidemiology, with particular interest in the principles and practices of evidence-based medicine."[64] He has also been the chair of several different randomized drug trials.[65] With these

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[61]For a good summary of the law pertaining to "custom" *see* PROSSER AND KEETON ON THE LAW OF TORTS § 33 (5th Ed. 1984); *See also*, RESTATEMENT (THIRD) OF TORTS § 13 (2005).

[62]Doc. No. 213.

[63]*Reeves v. Wyeth*, 4:05-CV-00163 (E.D. Ark.), July 14, 2006 Tr. at 169-70.

[64]Doc. No. 213.

[65]*Id.*

credentials, he is clearly qualified to testify about evidence-based medicine and the necessity of large randomized clinical trials to determine the risks and benefits of drugs.

1. Duplicity -- Defendant's position on duplicity is not convincing. First Dr. Sackett suggests the study should have been done in the 1970s and Dr. Gueriguian says it should have been done in the 1980s. Second, Plaintiff claims that although the testimony of Dr. Sackett and Dr. Gueriguian overlap, they both have their specialties and their opinions must be viewed together. Third, Plaintiff contends that she does not intend to ask them the same questions. If the testimony is too duplicative, I will intervene and encourage leaner presentations.

2. Type of Study -- Contrary to Defendant's position that Dr. Sackett didn't explain what type of study should have been conducted, Dr. Sackett contends that a WHI-type study was necessary and would have put Defendant on notice regarding the alleged lack of cardiac benefits.[66] I agree with Defendant that Dr. Sackett's opinion regarding the specifics of the study is vague. However, it seems to me that Dr. Sackett's vagueness goes to the weight of his testimony rather than its admissibility.

3. "Fit" -- Defendant's argument regarding "fit" lacks merit. Because evidence regarding cardiac benefits is relevant to this case, Dr. Sackett's testimony regarding testing for a cardiac benefit is admissible.

Obviously, Dr. Sackett is not qualified to testify about FDA standards, but Plaintiff concedes that he's not going to talk about that. Nor will Dr. Sackett be permitted to testify as to what Wyeth should have or could have done to be a leader in the industry.

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[66] *Id.*

F. Plaintiff's Motion to Preclude Defendant's Experts from Testifying That There is No Reliable Scientific Evidence that Combination Hormone Therapy Can Cause Breast Cancer (Doc. No. 193)

As with Defendant's objections to Plaintiff's causation experts, each argument appears to go to credibility, not admissibility, and can be raised on cross-examination.

G. Defendant's Motion for Summary Judgment Re: Specific Causation (Doc. No. 87)

Since Defendant's Motion to Exclude Expert Testimony of Drs. Klimberg and Waldron as to Specific Causation was denied, material facts remain in dispute as to causation.

CONCLUSION

Based on the findings of fact and conclusions of law made during the hearings and above:

1. Defendant's Motion to Exclude Expert Testimony of Drs. Klimberg and Waldron as to Specific Causation (Doc. No. 136) is DENIED.

2. Defendant's Motion to Exclude Expert Testimony of Dr. Hollon (Doc. No. 140) is DENIED, except as to the limitations mentioned above.

3. Defendant's Motion to Exclude Testimony of Dr. Gueriguian (Doc. No. 142) is DENIED, except as to the limitations mentioned above.

4. Defendant's Motion to Exclude Expert Testimony of Dr. Sackett (Doc. No. 144) is GRANTED regarding testimony about FDA standards and what Defendant could do to be a leader in the industry. The motion is DENIED regarding the remaining points.

5. Defendant's Motion to Exclude Expert Testimony of Dr. Austin (Doc. No. 148) is GRANTED as it concerns testimony regarding causation and DENIED as to the remaining points.

6. Plaintiff's Motion to Preclude Defendant's Experts from Testifying That There is No Reliable Scientific Evidence that Combination Hormone Therapy Can Cause Breast Cancer (Doc. No. 193) is DENIED.

7. Defendant's Motion for Summary Judgment Re: Specific Causation (Doc. No. 87) is DENIED.

Most of the arguments regarding exclusions of experts overlapped with the issues in *Reeves v. Wyeth* -- as evidenced by the fact that Ms. Rush filed identical responses to the motions to exclude as Ms. Reeves. For that reason, in this case, I have considered the positions that were argued by Ms. Reeves's counsel in subsequent oral argument and letter exchanges. However, if there are any *Daubert* issues that are unique to Ms. Rush, which are not addressed in this order, the parties should file the appropriate motion no later than 5 p.m., Thursday September 21, 2006.

IT IS SO ORDERED this 13th day of September, 2006.

/s/ Wm. R. Wilson, Jr.
UNITED STATES DISTRICT JUDGE

EXHIBIT 3

IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF ARKANSAS
WESTERN DIVISION

In re:	:	MDL Docket No. 4:03CV1507-WRW 4:04CV01169
PREMPRO PRODUCTS LIABILITY LITIGATION	:	
DONNA SCROGGIN	:	PLAINTIFF
v.	:	
WYETH, et. al.	:	DEFENDANTS

ORDER

Motion in Limine to Exclude Evidence of Wyeth's Net Worth (Doc. No. 571) -- is GRANTED --because I believe Professor Brill's analysis is correct. No evidence of net worth will be admissible.

Plaintiff's Objection to Evidence of General Goodness (Doc. No. 590). I will rule on this after opening statements. If the issue is not raised in opening statement, I'll rule at the close of Defendants' case as to whether Plaintiff can submit rebuttal evidence.

Defendants' Motions Exclude Testimony Re Total Excess Breast Cancer In Punitive Damages Stage (Doc. Nos. 569, 579) are DENIED. However, the parties should submit a limiting instruction per *Philip Morris*.

Defendant's Motion to Exclude Testimony of Dr. Matthew Hollon in Punitive Damages Phase (Doc. No. 567) is GRANTED.

Wyeth's Objection to Certain Designations by Plaintiff of Dr. Colditz's Testimony (Unrelated to Excess Breast Cancer) (Doc. No. 581) -- the rulings by Judge Jones on deposition designations for Colditz stand.

IT IS SO ORDERED this 3rd day of March, 2008.

/s/ Wm. R. Wilson, Jr.
UNITED STATES DISTRICT JUDGE

EXHIBIT 4

IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF ARKANSAS
WESTERN DIVISION

In re:	:	MDL Docket No. 4:03CV1507-WRW 4:04CV01169
PREMPRO PRODUCTS LIABILITY LITIGATION	:	
DONNA SCROGGIN	:	PLAINTIFF
v.	:	
WYETH, et. al.	:	DEFENDANTS

ORDER

Pending are Defendants' Motion to Exclude Expert Testimony of Dr. Robert Fincher (Doc. No. 105), Motion to Exclude Expert Testimony of Dr. Elizabeth Naftalis (Doc. No. 113), and Motion to Exclude Expert Testimony of Dr. Matthew Hollon (Doc. No. 109). Oral argument was heard on November 5-6, 2007, and the parties filed supplemental briefs and responses on November 9 and 11.[1]

Also at issue is Dr. Austin's testimony on the development of breast cancer at the cellular level, since Plaintiff filed a supplemental brief (Doc. No. 352).

I. STANDARD

A. Burden of Proof

The admission of expert testimony is governed by Rule 702 of the Federal Rules of Evidence, which reads:

[1]Doc. Nos. 342-345, 347.

> If scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue a witness qualified as an expert by knowledge, skill, experience, training, or education, may testify thereto in the form of an opinion or otherwise, if (1) the testimony is based upon sufficient facts or data, (2) the testimony is the product of reliable principles and methods, and (3) the witness has applied the principles and methods reliably to the facts of the case.[2]

When a party proffers an expert witness, deciding whether Rule 702 is satisfied is a preliminary issue governed by Federal Rule of Evidence 104(a).[3] Rule 104(a) requires the proponent of evidence to establish its admissibility by a preponderance of the evidence.[4] In determining admissibility, the court is not bound by any of the rules of evidence, except with regard to privilege.[5]

B. Legal Standard for Admissibility

The central inquiry under Rule 702 is whether the proffered expert's testimony is sufficiently reliable.[6] The trial court serves a gatekeeping function, ensuring that any expert testimony is reliable and relevant.[7]

To be admissible, expert testimony must satisfy the two prongs of Rule 702.[8] First, it must be based on scientific, technical, or other specialized knowledge.[9] If the testimony is

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[2] Fed. R. Evid. 702.

[3] *U.S. v. Martinez*, 3 F.3d 1191, 1196 n.10 (8th Cir. 1993).

[4] *Bourjaily v. U.S.*, 483 U.S. 171 (1987).

[5] Fed. R. Evid. 104(a).

[6] *First Nat'l Bank v. Benham*, 423 F.3d 855, 861 (8th Cir. 2005).

[7] *Id.*

[8] *U.S. v. Cawthorn*, 429 F.3d 793, 799 (8th Cir. 2005).

[9] *Id.*

scientific, it must be grounded in the methods and procedures of science.[10] Likewise, "knowledge" requires more than a subjective belief or an unsupported speculation, requiring instead an appropriate level of validation.[11] Second, the testimony must be relevant, in that it must help the trier of fact either understand the evidence or determine a fact in issue.[12] The burden of establishing relevancy and reliability rests on the proponent of the expert testimony.[13]

Courts have used a variety of factors to determine the reliability of proffered expert testimony. The most frequently discussed factors are those derived from the Supreme Court's opinion in *Daubert*, where the Court established that the trial court may consider:

> (1) whether the theory or technique can be or has been tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether the theory or technique has a known or potential error rate and standards controlling the technique's operation; and (4) whether the theory or technique is generally accepted in the scientific community.[14]

Because the inquiry is "flexible and fact-specific, a court should use, adapt, or reject *Daubert* factors" as needed based on the facts of a particular case.[15]

The most recent amendments to Rule 702 added three general standards for courts to use in determining the reliability and relevance of proffered expert testimony. First, the proffered testimony must be based on sufficient facts or data.[16] Second, it must be the product of reliable

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[10] *Id.*

[11] *Id.* at 799-800 (quoting *Daubert v. Merrell Dow Pharms.*, 509 U.S. 579, 590 (1993)).

[12] *Id.* at 799.

[13] *Moore v. Ashland Chem., Inc.*, 151 F.3d 269, 278-78 (5th Cir. 1998).

[14] *Benham*, 423 F.3d at 861 (citing *Daubert*, 509 U.S. at 593-94).

[15] *Unrein v. Timesavers, Inc.*, 394 F.3d 1008, 1011 (8th Cir. 2005).

[16] Fed. R. Evid. 702(1).

principles and methods.[17] Third, the expert must have applied those principles and methods reliably to the facts of the case.[18]

The focus is not on the expert's conclusion, but on the methodology.[19] The proponent of the testimony "need not prove . . . that the expert's testimony is correct, but . . . must prove by a preponderance of the evidence that the testimony is reliable."[20] Determining the validity of an expert's conclusions is the duty of the finder of fact.

II. ANALYSIS

A. Defendants' Motion to Exclude Expert Testimony of Dr. Robert Fincher (Doc. No. 105)

Dr. Fincher is Plaintiff's radiology/mammography expert. Plaintiff asked Dr. Fincher to review mammograms and determine whether "to a reasonable degree of medical probability, E+P had an effect on the density of Plaintiffs' breasts as measured by mammogram."[21] He also was asked to determine whether "based on the mammographic findings, E+P contributed to the development" of Plaintiff's breast cancer.[22]

Defendants contend that Dr. Fincher's opinions are not supported by reliable scientific evidence, are speculative, and are incomplete.[23]

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[17]Fed. R. Evid. 702(2).

[18]Fed. R. Evid. 702(3).

[19]*Moore*, 151 F.3d at 275-76.

[20]*Id* at 276.

[21]Doc. No. 177.

[22]*Id.*

[23]Doc. No. 106.

The motion is GRANTED in PART and DENIED in PART.

Dr. Fincher can testify generally about changes in breast density and the relationship, if any, between breast density and breast cancer risk. However, Dr. Fincher has not established, on this record, that changes in this Plaintiff's breast density, as related to HRT use, caused her cancer. Dr. Fincher's conclusions regarding any increase in Plaintiff's breast density after taking HRT lack reliability, because Dr. Fincher did not observe Plaintiff's pre-HRT mammograms. Even he concedes this point: "What I don't know is did it actually increase the degree of her breast density when she started taking the hormones, because there are no pre-hormone replacement therapy mammograms to compare."[24]

B. Defendants' Motion to Exclude Expert Testimony of Dr. Elizabeth Naftalis (Doc. No. 113)

Dr. Elizabeth Naftalis is Plaintiff's specific causation expert, who will testify that Plaintiff's ingestion of HRT was a substantial contributing factor in Plaintiff's development of hormone dependant breast cancer.[25]

Defendants assert that Dr. Naftalis's testimony should be excluded, because differential diagnosis is not a reliable method to determine the cause of Plaintiff's breast cancer, and Dr. Naftalis does not reliably apply her methodology to the facts of this case.[26]

I believe that Judge Wilson's rulings in the previous bellwether trials are on point, and I adopt them here. To paraphrase: while the report is somewhat conclusive, rather than

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[24]Fincher Dep., July 20, 2007 Tr. at 41, lines 9-13.

[25]Doc. No. 183, Ex. 1.

[26]Doc. No. 114.

explanatory, I cannot say that Dr. Naftalis used improper methodology. She is qualified to testify that HRT more likely than not promoted Plaintiff's breast cancer. Her conclusions can be tested during cross-examination.[27]

Accordingly, Defendants' Motion to Exclude Expert Testimony of Dr. Elizabeth Naftalis (Doc. No. 113) is DENIED.

C. Defendants' Motion to Exclude Expert Testimony of Dr. Matthew Hollon (Doc. No. 109)

Dr. Hollon is Plaintiff's marketing expert. Plaintiff asserts that Dr. Hollon will testify regarding "pharmaceutical marketing and its impact on the medical community . . . ."[28] Plaintiff contends that Dr. Hollon will "educate the jury on marketing strategies, effectiveness and how Wyeth used the loopholes in the FDA regulations . . . to influence and persuade physicians about the safety and effectiveness of E+P drugs."[29]

1. Liability Stage

As mentioned in Section I of this Order, the testimony must be relevant, in that it must help the trier of fact either understand the evidence or determine a fact in issue.[30] The burden of establishing relevancy, reliability, and necessity of Dr. Hollon's testimony rests on Plaintiff.[31]

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[27]See *In re Prempro, Reeves v. Wyeth*, No. 4:05-CV-00163, 2006 WL 2314062, at *3 (E.D. Ark. August 21, 2006) (citations omitted).

[28]Doc. No. 174.

[29]*Id.*

[30]*U.S. v. Cawthorn*, 429 F.3d at 799.

[31]*Moore v. Ashland Chem., Inc.*, 151 F.3d at 278-78.

Here, Plaintiff asserts that if, during trial, Judge Wilson admits evidence that shows reliance on certain marketing materials, Dr. Hollon's testimony *may* become relevant. At this point, Plaintiff is unable to show whether Dr. Hollon's testimony is relevant or aids the trier of fact in understanding the evidence. Dr. Hollon appears to be qualified as an expert in pharmaceutical marketing, in general, but whether he can render an opinion on specific marketing is tied to what evidence is introduced at trial.

At this stage, Dr. Hollon must have examined the evidence necessary to form his expert opinion. Also, Plaintiff should be able to identify the marketing or promotional materials they believe would be admissible under Judge Wilson's previous rulings regarding reliance and marketing evidence. Instead, Plaintiff attempts to condition Dr. Hollon's opinions on evidence that *may* become available at trial.

Plaintiff concedes Dr. Hollon's opinions are based on what may become available during trial. Without the specific fact, data, or other evidence necessary for Dr. Hollon's opinion, I must GRANT Defendants' Motion to Exclude Expert Testimony of Dr. Matthew Hollon (Doc. No. 109), at this time.

2. Punitive Damages Stage

Judge Wilson previously addressed the issue of the admissibility of Dr. Hollon's testimony at the punitive damages stage, if there is one:

> It seems to me that any evidence of Defendant's "badness" during the punitive damage portion of the trial (if there is one) must be connected to Ms. Reeves's injury. However, the nexus between Plaintiff and the advertisements need not be as strong as the causation requirements during the liability stage of the trial. Dr. Hollon can testify regarding advertisements -- however, those advertisements must pertain to issues that are directly linked to Plaintiff, e.g., cardiac benefit, breast cancer, etc.

> Dr. Hollon will not be permitted to testify regarding general badness or badness in the specific areas which are not connected to Ms. Reeves's injury.[32]

The Supreme Court held that:

> Evidence of actual harm to nonparties can help to show that the conduct that harmed the plaintiff also posed a substantial risk of harm to the general public, and so was particularly reprehensible-although counsel may argue in a particular case that conduct resulting in no harm to others nonetheless posed a grave risk to the public, or the converse. Yet for the reasons given above, a jury may not go further than this and use a punitive damages verdict to punish a defendant directly on account of harms it is alleged to have visited on nonparties.

Philip Morris U.S.A. v. Williams, 127 S. Ct. 1057, 1064 (2007).

Judge Wilson's ruling is still appropriate.

D. Dr. Austin Cellular Testimony

The November 9, 2007 Order noted that I could find nothing in the record regarding Dr. Austin's testimony on the development of breast cancer at the cellular level. Plaintiff supplemented the record on November 13, 2007. Based on this supplement, I am convinced that Dr. Austin can testify on this issue. The November 9, 2007 Order is VACATED to the extent that it granted Defendants' motion to exclude Dr. Austin's testimony regarding development of breast cancer at the cellular level. Accordingly, the motion is DENIED on this point.

IT IS SO ORDERED this 15th day of November, 2007.

Henry L. Jones, Jr.
UNITED STATES MAGISTRATE JUDGE

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[32] *In re Prempro, Reeves v. Wyeth*, No. 4:05-CV-00163, 2006 WL 2314062, at *5 (E.D. Ark. August 21, 2006) (citations omitted).

EXHIBIT 5

IN THE CIRCUIT COURT OF THE SIXTH JUDICIAL CIRCUIT
IN AND FOR PINELLAS COUNTY, FLORIDA
CIRCUIT CIVIL NO. 05-1606-CI-13

PETER ESPOSITIO, individually and as Personal Representative of the Estate of LORETTA ESPOSITO,

Plaintiff,

Vs.

WYETH, INC., and WYETH PHARMACEUTICALS, INC., and ESI LEDERLE; CAROL BANKS; and MARY TATE,

Defendants.
_____/

ORDER GRANTING DEFENDANTS' MOTION IN LIMINE TO BAR THE MARKETING PRACTICES TESTIMONY OF DR. MATTHEW HOLLON

THIS CAUSE came before the court upon Defendants' Motion in Limine to Bar the Marketing Practices Testimony of Dr. Matthew Hollon, the court having heard argument of counsel and being otherwise fully advised in the premises, it is thereupon

ORDERED AND ADJUDGED that said motion be and the same is hereby granted.

DONE AND ORDERED in Chambers at St. Petersburg, Pinellas County, Florida, this _____ day of April, 2010.

ANTHONY RONDOLINO, Circuit Judge

Copy furnished to:
Edward W. Gerecke, Esq.
James D. Clark, Esq.
Tobias Millrood, Esq.
Chen-Sen Wu, Esq.
Rebecca Moos, Esq.
George E. McDavid, Esq.
Robert K. Jenner, Esq.
James F. Szaller, Esq.

EXHIBIT 6

IN THE UNITED STATES DISTRICT COURT FOR THE
EASTERN DISTRICT OF VIRGINIA
Alexandria Division

GEORGIA TORKIE-TORK, Plaintiff,	)	
v.	)	CIVIL ACTION
WYETH, Defendant.	)	1:04-cv-945

REPORTER'S TRANSCRIPT

MOTIONS HEARING

Monday, November 15, 2010

BEFORE: THE HONORABLE T.S. ELLIS, III
Presiding

APPEARANCES: LITTLEPAGE BOOTH
BY: ZOE LITTLEPAGE, ESQ.
RAYMOND BOOTH, ESQ.
2043A W. Main St.
Houston, TX 77098

KOPSTEIN & PERILMAN
BY: PHILIP KULJURGIS, ESQ.
8633 Cross Chase Ct.
Fairfax Station, VA 22039

For the Plaintiff

MICHAEL A. RODRIQUEZ, RPR/CM/RMR
Official Court Reporter
USDC, Eastern District of Virginia
Alexandria Division

APPEARANCES (Continued):

PAUL, WEISS, RIFKIND, WHARTON & GARRISON, LLP
BY: BETH WILKINSON, ESQ.
BRIAN STEKLOFF, ESQ.
2001 K Street, NW
Washington, DC 20006-1047

WILLIAMS & CONNOLLY, LLP
BY: RYAN SCARBOROUGH, ESQ.
725 12th St NW
Washington, DC 20005

For the Defendant

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(Court recessed)

ATTORNEY WILKINSON: Your Honor, I believe you were asking us about whether you ruled on all the Daubert, and that is what I was trying to address. I'm sorry to re-raise Dr. Michaels.

THE COURT: Yes.

ATTORNEY WILKINSON: Dr. Blume and Dr. Parisian, I don't think you gave us a ruling on. And there are some others.

THE COURT: And then what?

ATTORNEY WILKINSON: There are a few others. Dr. Bollon and -- oh, they had had a motion to exclude Dr. Acs.

And we have a motion to exclude Dr. Patton, their radiologist.

THE COURT: Holton, or is it Bollon?

ATTORNEY LITTLEPAGE: Bollon.

THE COURT: Bollon intends to testify that Wyeth's marketing practices were misleading and he will compare branded and unbranded ads.

Of course he can't testify to Wyeth's intent. That would be inadmissible, speculative.

As far as him testifying about branded and unbranded ads, Ms. Littlepage, you may certainly put on -- introduce the branded and unbranded ads, but I don't think this is a 702 matter.

Experts don't need to be adduced to show that the typeface is the same or the colors are the same or to make arguments from them. This is typical of a situation where an expert is used to confer on evidence that a jury can understand. Greater dignity. And I don't think it's warranted.

So, I don't think this is methodology that warrants being assessed. There is no methodology looking at two ads, branded and unbranded ads. And the unbranded ads discuss adverse cardiac and neurological symptoms of menopause without mentioning Prempro.

Then in a separate branded ad, Wyeth discusses how Prempro alleviates menopausal symptoms. They have similar colors, layouts, styles.

And so Hollon says that Wyeth hopes readers will connect the branded and unbranded ads to conclude Prempro cures the relevant symptoms. I will exclude that testimony.

That doesn't mean you can't use the ads that you want to in some way, but it's not worthy of an expert.

Then we come to Randall Patton. This one is a live witness, isn't he, Ms. Littlepage?

ATTORNEY LITTLEPAGE: Yes, sir.

THE COURT: All right. Let's find a time -- let me review his, because there may be one or two things I

EXHIBIT 7

IN THE UNITED STATES DISTRICT COURT FOR THE
EASTERN DISTRICT OF VIRGINIA
Alexandria Division

GEORGIA TORKIE-TORK,	)	
	)	
Plaintiff,	)	
	)	
v.	)	CIVIL ACTION
	)	
WYETH,	)	1:04-cv-945
	)	
Defendant.	)	
	)	

REPORTER'S TRANSCRIPT

JURY TRIAL

VOLUME 1

Tuesday, November 16, 2010

BEFORE: THE HONORABLE T.S. ELLIS, III
Presiding

APPEARANCES: LITTLEPAGE BOOTH
BY: ZOE LITTLEPAGE, ESQ.
RAYMOND BOOTH, ESQ.
2043A W. Main St.
Houston, TX 77098

KOPSTEIN & PERILMAN
BY: PHILIP KULJURGIS, ESQ.
8633 Cross Chase Ct.
Fairfax Station, VA 22039

For the Plaintiff

MICHAEL A. RODRIQUEZ, RPR/CM/RMR
Official Court Reporter
USDC, Eastern District of Virginia
Alexandria Division

APPEARANCES (Continued):

PAUL, WEISS, RIFKIND, WHARTON & GARRISON, LLP
BY: BETH WILKINSON, ESQ.
BRIAN STEKLOFF, ESQ.
2001 K Street, NW
Washington, DC 20006-1047

WILLIAMS & CONNOLLY, LLP
BY: RYAN SCARBOROUGH, ESQ.
725 12th St NW
Washington, DC 20005

For the Defendant

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WITNESS (Plaintiff)	DIRECT	CROSS	REDIRECT	RECROSS
Frederick Smith	293	314	331	---

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(Court recessed)

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prescribing doctors relied on it. I think that's right. If they actually relied on certain marketing materials, the prescribing doctors, then it would be relevant and admissible.

But the plaintiff must demonstrate actual reliance for it to be relevant. If plaintiff's doctors say that they usually or sometimes read marketing material and rely on it, then the probative value of that evidence is substantially outweighed by the danger of unfair prejudice, confusion, and a waste of time.

If their testimony is that they always read all marketing material and relied on it, then possibly that evidence might may have some probative value. But it may still be cumulative for a number of reasons.

At least one of the plaintiff's doctors states that he relied on the label. If statements in the marketing material add nothing to the statements already made on the Prempro label, then the introduction of the marketing material is cumulative and not admissible.

If the marketing material adds new information, then only if that new information must take off-label benefits, for example, if that was relied on by the prescribing doctors, then that may be admissible.

Let's take, for example, off-label benefits of heart or cardiovascular benefits that are reflected in

EXHIBIT 8

Report of Matthew F. Hollon, MD MPH

Summary of Professional Background

My name is Matthew Hollon. I am a board certified physician of Internal Medicine at the University of Washington in Seattle (UW). I was graduated from the UW School of Medicine (1994). Following my graduation, I completed my residency (1997) and fellowship in Internal Medicine (1999), also at UW. While completing my fellowship, I simultaneously attended the UW School of Public Health and Community Medicine where I received a Masters of Public Health (1999).

I currently am Director of Evidence-Based Medicine for the Internal Medicine Residency Program at the UW Department of Medicine and an Assistant Professor in the Division of General Internal Medicine.

Nationally I have been an active member in professional organizations including The Society of General Internal Medicine and The American College of Physicians. Internationally, I have served as a Member of an Expert Advisory Panel on the Assessment of the Health System Impacts of Direct-To-Consumer Advertising of Prescription Medicines – a Report to Health Canada.

I have conducted independent social science research and written evidenced-based reviews and editorials as a part of my responsibilities at UW. Some of my publications which have particular relevance to the topic of pharmaceutical advertising of hormone therapy, the matter which I will address below, include:

1. Hollon MF. Direct-to-consumer advertising - A haphazard approach to health promotion. JAMA. 2005;293(16):2030-3.
2. Hollon MF. Direct-to-consumer marketing of prescription drugs: A current perspective for neurologists and psychiatrists. CNS Drugs. 2004;18(2):69-77.
3. Hollon MF, Larson EB, Koepsell TD, Downer A. Direct-to-consumer marketing of

osteoporosis drugs and bone densitometry. Annals of Pharmacotherapy. 2003;37(7/8):976-981.

4. Hollon MF. Direct-to-consumer marketing of prescription drugs: Creating consumer demand. JAMA. 1998;281(4):382-384.
5. Hollon MF. Treatment Basics. In OsteoEd (Osteoporosis Education). Laya M, Migeon M, eds. Available at http://www.osteoed.org.
6. Hollon MF. Selective Estrogen Receptor Modulators in Osteoporosis. In OsteoEd (Osteoporosis Education). Laya M, Migeon M, eds. Available at http://www.osteoed.org.

I lecture on areas of my expertise. Some relevant lecture topics include:

1. Wong CJ, Hollon MF, Teraski G. Evidence Based Medicine Seminar for Internal Medicine Residents. Abstract for Society for General Internal Medicine's 28th Annual Meeting. New Orleans, LA. May 2005.
2. Wong CJ, Hollon MF, Teraski G. Evidence Based Medicine Seminar for Internal Medicine Residents. Plenary Session Presentation for Society for General Internal Medicine's Northwest Regional Meeting. Vancouver, WA March 11, 2005.
3. Hollon MF. Direct-to-consumer marketing of prescription drugs and health service utilization. Presented at The 22nd Annual Meeting of The Society of General Internal Medicine. San Francisco, CA. April 29 – May 1, 1999.

Among my current research projects include participation in a submitted grant from UW School of Pharmacy to fund a Regional Center to evaluate, in part, the ongoing impact of Direct to Consumer (DTC) marketing of prescription drugs.

My fee for consultation and preparation of reports is $300 per hour. My fee for travel time, depositions, and trial testimony is $350 per hour.

I have not served as an expert witness within the past five years and, thus, have given no depositions or sworn trial testimony.

Summary of Opinions

In my professional opinion, drawing on my background, training, education and experience generally, and in particular my work as Director of Evidenced-Based Medicine for an Internal Medicine residency program, and, last but not least, a practicing primary care physician committed first and foremost to the welfare of my patients, based on the case below, I come to the following conclusions. Wyeth-Ayerst Laboratories:

1. In the words of CEO Bob Essner, led "a crusade more than a typical pharmaceutical effort"[1] in making the Premarin family of drugs a $2 billion per year commodity for a condition, menopause, that was not undertreated.
2. Accomplished this first and foremost by expert marketing relying on expanding the perception that hormone therapy is appropriate for every menopausal woman and utilizing aggressive integrated marking tactics targeting physicians and patients together as the "consumer" such that physicians would prescribe hormone supplementation in the face of patient requests.
3. Persuaded the medical community and the public that healthy, asymptomatic menopausal women should take hormones for an ever expanding list of symptoms by manufacturing data, purchasing professional opinions, and utilizing the entire catalogue of possible promotional activities based on often misleading and unbalanced marketing schemes that over zealously relied on purported but often unfounded benefits.
4. Started inappropriately and continued over several decades a "start her on, keep her on" marketing strategy without scientific support for long-term use eventually ignoring sound epidemiologic principles by unreasonably pushing hormone supplementation for population prevention (in the face of reasonable alternative therapies) in all menopausal women beginning early in menopause when these women, on average, were more likely to suffer harm than realize the minimal benefit.
5. Systematically ignored or minimized unfavorable scientific evidence and, thus, failed to adequately warn physicians and patients of the risks of hormone supplementation.
6. Eroded the traditional role of the physician as a "learned intermediary" by marketing efforts that knew "no boundaries, no limits."[2]
7. Nearly seamlessly, from a historical perspective, transitioned women from an early strategy of unopposed estrogen to combination estrogen and progestin supplementation for women who had not had a hysterectomy (the largest percentage of menopausal women) eventually "cannibalizing Premarin with the continuous HRT regimen, Prempro".[3]

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[1] 4/4 10AM. Bob Essner. Day 3 Close.
[2] 4/4 10AM. Bob Essner. Day 3 Close.
[3] LUDMG002-001710.

8. Should have reserved hormone supplementation for short-term use or for those women at the highest risk of suffering a fracture as a consequence of osteoporosis, specifically much older women or women with multiple risk factors for developing the disease, and tailored their marketing campaign accordingly.

Method To Evaluate Reasonable Promotion

Do the benefits of an integrated promotional campaign outweigh the danger that consumers will demand and take medicines inappropriately? Three factors determine the health impact of promotional campaigns for any given drug: 1) the current prevalence of under-treatment; 2) the amount of inappropriate prescribing stimulated by promotional efforts; and 3) the degree of harm accruing to under-treated compared with over-treated patients.[4] The fulcrum of this equilibrium largely rests on the quality of the information provided by the promotional material about the drug and the characteristics of the population targeted for receiving the drug. Furthermore, the accelerated use of the marketing strategies targeting physicians and patients together exposes a large number of patients to medications whose harms may only emerge after long induction periods. This fact, in and of itself, means a pharmaceutical company must be exceedingly cautious in selling its drug products (particularly when those drug products are known carcinogens) prior to an adequately completed research agenda when the likely benefit to any individual patient is small.

As I will analyze and conclude below, Wyeth irresponsibly failed to meet a reasonable standard of care for drug promotion, utilizing in excess the full catalogue of promotional strategies and activities to sell its menopausal hormonal supplementation program over several decades to all menopausal women, some of whom were harmed as a direct result.

[4] Hollon MF. *Direct-to-consumer marketing of prescription drugs: A current perspective for neurologists and psychiatrists.* CNS Drugs 2004;18(2):69-77.

In summary, compelling evidence suggests that there are only three clinically significant consequences of menopause that should drive therapeutic considerations. These are hot flashes, vaginal dryness, and loss of bone mass in elderly women at high risk of fracture.

Historical Usage of Hormones in Menopause

As a physician who has researched, published and lectured on the topic of pharmaceutical advertising, my opinions about Wyeth's improper promotion of hormone therapy and their success in manufacturing a conventional wisdom about menopausal hormone supplementation must be understood in the context of the historical underpinnings that gave rise to their comprehensive marketing scheme. Understanding the historical framework of hormone therapy's development is critical to understanding how these pharmaceutical companies created consumer demand. Indeed, Wyeth ultimately used the historical context of menopause and hormone therapy to its advantage in marketing the Premarin family to physicians and patients.

Significant commercial use of hormones in menopause began with the discovery and production of sex hormones in the 1930's.[22] Looking for a reasonably potent, low cost source of estrogens, Ayerst Laboratories settled on extracting the chemical from pregnant mares' urine and eventually dubbed the product Premarin.[23] On January 17, 1939, the first gallon of this water-soluble estrogenic complex was processed at the Ayerst Laboratories.[24] Investigations revealed that a stable, active preparation of estrogenic conjugates could indeed be made and that the material showed high oral activity. After two years of work, Premarin was ready to be marketed

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[22] Krieger N, Lowy I, Aronowitz R, et al. *Hormone replacement therapy, cancer, controversies, and women's health: historical, epidemiological, biological, clinical, and advocacy perspectives.* J Epidemiol Community Health. 2005;59(9):740-8.

[23] BURRG002-000050 (10/31/94)

[24] Anonymous. *Premarin: Discovery of First Orally Active Estrogen.* Canada's Digital Collections, Heirloom Series, Vol. 6. Available at http://collections.ic.gc.ca/heirloom_series/volume6/290-291.htm. Accessed January 23, 2006.

Promotion to health care providers

Traditionally, drug companies have promoted their products directly to health care providers. The foundation of marketing strategies have centered on company representatives or "detail persons" who visit individual physicians and provide promotional information on products. In 2001, this sales force numbered nearly 90,000 in the US – approximately 1 salesperson for every 5 physicians.[56] Studies suggest that over 80% of doctors see these drug company representatives on average once per week and that prescribing habits are less appropriate as a result.[57,58] While industry proponents assert that detailing raises awareness of products that benefit patients, Katz et al counter that there is no published evidence to support this claim.[59] Katz et al go on to write, "In contrast, research suggests that physicians rely heavily on detailers for information and that the more doctors rely on commercial sources of information the less likely they are to prescribe drugs in a manner consistent with patient needs."[60]

Other overt promotional strategies have included advertising directly to providers in medical journals, sponsoring scientific symposia and continuing medical education (CME), direct-mailing of promotional materials, and providing free samples of medication.[61,62,63,64]

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[56] Blumenthal D. *Doctors and Drug Companies.* N Engl J Med 2004;351:1885-90.
[57] Moynihan R. *Who pays for the pizza? Redefining the relationships between doctors and drug companies. 1:Entanglement.* BMJ 2003;326:1189-92. Moynihan notes that there is evidence that the information drug representatives present is "overly positive".
[58] Wazana A. *Physicians and the pharmaceutical industry. Is a gift ever just a gift?* JAMA 2000;283(3):373-80.
[59] Katz D, Caplan AL, Merz JF. *All gifts large and small. Toward an understanding of the ethics of pharmaceutical industry gift giving.* Am J Bioeth 2003;3(3):39-46.
[60] Ibid. Further substantiating Moynihan's position about the quality of the information drug representatives provide, Katz et al cite three studies noting that information provided by detailers if often biased and sometimes dangerously misleading.
[61] Kessler DA, Pines WL, op cite.
[62] Palmlund I. *The marketing of estrogens for menopausal and postmenopausal women.* J Psychosom Obstet Gynecol 1997;18:158-64.
[63] Groves KE, Sketris I, Tett SE. *Prescription drug samples--does this marketing strategy counteract policies for quality use of medicines?* J Clin Pharm Ther. 2003;28(4):259-71. This comprehensive review concludes that more research into the effect of prescription drug samples on prescribing is needed but it does draw out the negative impact of prescription drug sampling on a number of factors.

Indeed, CME courses sponsored by the pharmaceutical industry are now one of the most frequent ways the industry interacts with and influences practicing physicians.[65] In 2000, for example, the industry sponsored 314,000 events specifically for physicians.[66] As of 2003, according to Dr. Murray Kopelow, president of the Accreditation Council for Continuing Medical Education, pharmaceutical companies were providing about $900 million of the $1 billion spent annually on CME in the United States.[67]

Studies of medical journal advertisements directed at physicians have revealed that claims made in these advertisements are based on poorly substantiated evidence. In one study, Wade et al asked pharmaceutical companies to supply their best evidence in support of marketing claims.[68] Of 67 references cited, only 31 contained relevant original data and only 13 were controlled trials. These investigators concluded, "Standards of evidence used to justify advertising claims are inadequate." A recent study reviewed 438 unique ads from the 1999 issues of 10 American medical journals and a random sample of 400 references in medical research articles selected from the same journals. The authors summarize their findings, "Many pharmaceutical ads contain no references for medical claims. The majority of unpublished data-on-file references were not available and the majority of original research cited to substantiate claims in the pharmaceutical ads was funded by or had authors affiliated with the product's manufacturer."[69] Furthermore, the educational content of advertisement directed at providers is

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[64] Adair RF, Holmgren LR. *Do drug samples influence resident prescribing behavior? A randomized trial.* Am J Med. 2005;118(8):881-4. This randomized study of access to drug samples in clinic found that it influences resident prescribing decisions.
[65] Blumenthal D, op cite.
[66] Brennan TA, Rothman DJ, Blank L, et al. *Health industry practices that create conflicts of interest: a policy proposal for academic medical centers.* JAMA. 2006;295(4):429-33
[67] Blumenthal D, op cite.
[68] Wade VA, Mansfield PR, McDonald PJ. *Drug companies' evidence to justify advertising.* Lancet. 1989;2(8674):1261-3
[69] Cooper RJ, Schriger DL. *The availability of references and the sponsorship of original research cited in pharmaceutical advertisements.* CMAJ. 2005;172(4):487-91.

generally poor.[70,71,72] In general, the pharmaceutical industry designs these advertisements to trigger decision making shortcuts such as "newer is better" or "popular is better" that often enable busy doctors to reach quick but potentially erroneous conclusions.

The full catalogue of promotional activities that the industry uses to educate and influence health care providers, however, is much broader. It includes the offering of a vast array of gifts from token items to travel and more, the sponsoring of dinners and social events, the sponsoring of primary research, direct funding for academic chairs and lecture halls, the subsidizing of professional societies and associations, sponsoring and advising disease foundations or patients' groups, developing or supporting the development of clinical guidelines, providing membership to company advisory boards then paying these consultants as "thought leaders", soliciting "ghostwritten" scientific articles, and sponsoring medical journal supplements.[73,74] A substantial body of theoretical and empirical literature suggests that these promotional efforts by drug companies affect prescribing behavior as well.[75]

Gifts, used by the pharmaceutical industry for almost a century to promote specific products and establish brand recognition, may powerfully influence physician prescribing

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[70] Herxheimer A, Lundborg CS, Westerholm B. *Advertisements for medicines in leading medical journals in 18 countries: a 12-month survey of information content and standards.* Int J Health Serv 1993;23(1):161-72. In a study of advertising in the leading medical journals in 18 countries, Herxheimer et al reported that important warnings and precautions were missing in half of the 6700 advertisements surveyed.

[71] Stryer D, Bero LA. Characteristics of materials distributed by drug companies. An evaluation of appropriateness. J Gen Intern Med. 1996;11(10):575-83. Stryer and Bero concluded that advertisement contained a higher proportion of promotional material than educational material and little of this material contained information about important therapeutic breakthroughs.

[72] Wilkes MS, Doblin BH, Shapiro MF. *Pharmaceutical advertisements in leading medical journals: experts' assessments.* Ann Intern Med. 1992;116(11):912-9. In 1992, Wilkes et al evaluated 109 pharmaceutical advertisements and found that 57% of these advertisements had little or no educational value.

[73] Moynihan R, op cite. As Moynihan notes, "According to an article on the 'tricks of the trade', the advisory process is one of the most powerful means of getting close to [providers] and influencing them.

[74] Blumenthal D, op cite. Blumenthal notes, "As many as 59% of the authors of clinical guidelines endorsed by many professional associations have had financial relationships with companies whose drugs might be affected by those guidelines."

[75] Ibid.

behavior.[76] Every year, doctors receive multiple gifts, both large and small, from drug companies and most doctors deny their influence despite considerable evidence to the contrary.[77] Blumenthal highlights, "The idea that small gifts may be as influential as large gifts seems counterintuitive but is supported by substantial research in social science."[78] Katz et al explain this, noting, "The social rule of reciprocity imposes on the recipient an obligation to repay for favors, gifts, invitations, and the like. . . If physicians are to reciprocate for small gifts, they cannot do so in any form they please. They are essentially compelled to reciprocate by supporting their benefactor's products."[79]

A comprehensive summary by Wazana published in 2000 in the *Journal of the American Medical Association* reviews studies of a broad array of pharmaceutical industry-physician interactions.[80] Consistently across these studies interactions were associated with changes in physicians' use of medications. In general, industry interactions correlate with doctors' preferences for new products that hold no demonstrated advantage over existing ones, with a decrease in the prescribing of generics, and with a rise in both prescription expenditures and irrational, incautious prescribing.[81]

Over the last decade, there has been growing skepticism about the positive impacts of promotion of prescription drugs to health care providers resulting in substantial efforts to counteract the industry's access and messages to health care providers. Growing professional discomfort with the nature, extent, and potential consequences of interactions between physicians and pharmaceutical companies has led several professional societies to develop

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[76] Katz D, Caplan AL, Merz JF, op cite.
[77] Moynihan R, op cite.
[78] Blumenthal D, op cite.
[79] Katz D, Caplan AL, Merz JF, op cite.
[80] Wazana A, op cite.
[81] Moynihan R, op cite.

It is my opinion, to a reasonable degree of professional certainty, that Wyeth-Ayerst failed to meet usual standards of promotion and was directed to do so at the highest level of the organization when the CEO spoke of a "crusade" its sales force should embark on with "no boundaries, no limits."[152] The standards of reasonable and responsible promotion to which Wyeth failed to adhere included but were not limited to:

1. Grants . . . are not used to influence a physician or other health care provider in his or her prescribing habits or be based on the physician's prescribing practices e.g. to reward a high volume prescriber or product advocate;[153]
2. Continuing education is an independent non-promotional educational program;[154]
3. Visiting Speaker Programs use company-approved professional speakers to deliver Company Directed Educational Programs that are within product labeling.[155]
4. Drug promotion should not be false or misleading.
5. Promotional campaigns target only those for whom benefits of therapy clearly outweigh the harm, particularly when promoting a drug for prevention.
6. Promotional campaigns are based on scientific information of the highest standards.
7. Information is presented in a way that achieves fair balance between benefits and risks, adhering to standards to adequately disseminate and share information specifically about risk that would fairly balance discussions that patients had with their physicians.

This failure to comply with this last standard did not occur for a lack of a standard, but rather as a choice to systematically ignore or dismiss unfavorable science. Victoria Kusiak, Vice President, Global Medical Affairs, Wyeth-Ayerst agreed in her sworn testimony that it was a top objective of Wyeth to get women and physicians the information they need to make informed choices about all of its products, including the women's health care products.[156] I agree with Dr.

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[152] 4/4 10AM. Bob Essner. Day 3 Close. Plaintiff's exhibit 40.
[153] GOLDG001-001438 at page 1440.
[154] GOLDG001-001438 at page 1441.
[155] GOLDG001-001438 at page 1442
[156] Kusiak deposition 0196 6-18.

Kusiak's assessment of the appropriate obligation of a pharmaceutical company. This is the appropriate standard by which Wyeth should be evaluated.

The obligation to only target promotional campaigns at patients who can be certain of receiving more benefit than harm can be found in a number of Wyeth documents, including a letter from Wyeth-Ayerst North American President, Joe Mahady. In this letter he recognizes that Wyeth had a "special responsibility based on the nature of the products we sell and the patients who take them."[157] Pharmaceuticals have both the power to help, if used appropriately, and harm, if not. Based on this "special responsibility," Mahady directed his sales force to, "maintain the highest standards of compliance with respect to issues of product safety, medical education, use of approved materials and our promotion practices."[158] I agree with his declaration that drug companies have a special responsibility. Indeed, the medical community has urged companies to provide honest, accurate, and complete information about the benefits and risks in drug advertisements as it is necessary to serve the interests of physicians and the public.[159] Yet, this was not the directive the company followed, rather Wyeth-Ayerst modeled its marketing efforts on "a crusade more than a typical pharmaceutical effort."[160]

Again, Wyeth understands what the obligations of a reasonable pharmaceutical company were, as they sought to have those obligation enforced on competitors. A correspondence from 1989 highlights that Wyeth-Ayerst considered regulatory action against Mead Johnson on its Estrace promotion, lipids and lipoproteins. However, as "the promotion of the cardiovascular effects of Premarin is of critical importance to Wyeth-Ayerst and our approaches to date . . . do indeed push the edge of the envelope," the company concluded that they would have "more to

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[157] DEYMI015-000644. Joseph Mahady Letter January 2001.
[158] DEYMI015-000644.
[159] Woloshin S, Schwartz LM, TremmelJ, Welch HG. *Direct-to-consumer advertisements for prescription drugs: What are Americans being sold?* Op cite.
[160] 4/4 10AM. Bob Essner. Day 3 Close. Plaintiff's exhibit 40.

lose if our ability to discuss cardiovascular issues is limited than we have to gain from stopping the use of this particular Estrace promotion."[161,162] Wyeth clearly recognized the irresponsibility of promoting cardiovascular benefit in the absence of such an indication. It is my opinion that such promotion was not "pushing the envelope" as stated by Wyeth, but rather was violating reasonable and accepted standards of care owed to the consumer of hormone therapy.

Based on my professional expertise as clinician as well as my background, training, and education, and the available evidence-base which I reviewed, responsible promotion of hormone replacement should have included marketing the therapy to selected minority of women suffering moderate to severe vasomotor symptoms and then only for short-term use.[163] Reasonable promotion adhering to an acceptable standard of care should also have: 1) highlighted the risk of developing postmenopausal osteoporosis; 2) advocated for early primary prevention strategies such as regular exercise, calcium supplementation, and vitamin D supplementation and; 3) targteted hormone supplementation only to those with accelerating osteopenia (based on bone density testing) or otherwise at risk of developing clinically significant osteoporosis. Simply, Wyeth should have promoted hormone supplementation in the fraction of the older post-menopausal population at significant risk for hip fracture. Reasonable promotion would have adhered to the 1995 Wyeth Premarin Product Training Program manual recommending, "[hormone therapy] should be used where beneficial in the lowest effective therapeutic dose for the shortest period of time that satisfies the therapeutic

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[161] CONNS005000396

[162] In the wake of WHI, Wyeth-Ayerst no longer felt restrained in pursuing regulatory action against other manufacturers of menopausal hormone therapy including the so called "bio-identical hormone replacement". For good examples of the "pot calling the kettle black" see KUSIV009-009208 and Botha Sarah E. *Submission of Citizen Petition on Behalf of Wyeth.* Wiley, Rein, & Fielding. October 6, 2005. The standards Wyeth-Ayerst sets out in these documents are reasonable standards yet the irony is the Wyeth-Ayerst failed to adhere to them even though they were aware of them.

[163] Atrophic vaginitis and associated vaginal dryness are best treated with local rather than systemic therapy.

need."[164] Wyeth failed to follow these standards despite admonishment from the FDA, and instead, as mentioned above, at the directive of Bob Essner, pursued marketing campaigns that knew, "no boundaries, no limits".[165]

Wyeth knew that reasonable standards of promotion existed for the development of DTC material as well. The FDA had set out such expectations in correspondence with Wyeth. Examples of FDA admonishments that, in general, Wyeth ignored include a letter from February 1991. David Banks of the FDA writes, "The statement 'Keep your life after menopause as vital and healthy as ever. . .' Among the inferences to be derived from this claim is that ERT is essential to health and vitality. This is an inference with which we disagree."[166] Notably, in 2000, using celebrity spokesperson Lauren Hutton, Wyeth ran a DTC marketing scheme called the "Vitality" campaign.[167]

Later in February 1991, the FDA also took issue with promotional aspects of the *Seasons* magazine.[168] The FDA clearly laid out the rationale for considering the magazine promotional material then notes that, "the presentation of the magazine itself is misleading in that the sponsorship is not clearly stated."[169] The FDA goes to address specific content issues, among others:[170,171]

> . . . Clearly, Wyeth-Ayerst is not an unbiased independent source of information about its products. . .
>
> The discussion of menopause predisposing a woman to irritability and moodiness might mislead the reader to assume that if the 'hormonal upheaval' is treat with

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[164] W-MDL04782-00047468 at page 47492.
[165] 4/4 10AM. Bob Essner. Day 3 Close. Plaintiff's exhibit 40.
[166] W-MDL04782-00150936. Other admonishments include promoting unfound psychiatric benefits which Wyeth subsequently ignored in promotional campaigns that advertise emotional labiality as a symptom of menopause.
[167] SINAM001-000085 at page 93.
[168] W-MDL04782-000002391.
[169] W-MDL04782-000002391.
[170] W-MDL04782-000002391.
[171] W-MDL04782-00035765. Wyeth responded to the FDA in a letter making changes to bring this promotional material into line with rules and regulations but in subsequent marketing campaigns promoted psychiatric and cardiovascular benefits despite having already been admonished by the FDA.

> Premarin, the irritability and moodiness will be treated as well. This is not an approved indication.
>
> The fourth letter discussed cholesterol, fats, etc. We have concern that the issue of the magazine in which this letter would appear would discuss or imply the use of Premarin to decrease cardiovascular events in postmenopausal women. Since this type of indication is not an approved indication for the product, this would potentially cause Premarin to be misbranded.

Of course, in subsequent years, the promotion by Wyeth of the cardiovascular benefits of the Premarin family of drugs would continue unabated.

Just over one year later, the FDA again takes issue with Wyeth's attempts to expand the perceived benefits noting, "the chart shows part of the effects of the climacteric as skin atrophy and atherosclerosis. While these may be seen as outcomes of the climacteric, they are misleading when used in the context of a Premarin advertisement."[172] The letter continues, "The language sheets discuss changes in cholesterol levels which occur in the menopause. . . implying that estrogen TREATS cholesterol changes. In addition, there is a further implication that there is cardiovascular benefit with Premarin use inherent in such a discussion."[173]

Another letter from July 1992 finds Wyeth-Ayerst continuing to push the cardiovascular benefit, "the information in the booklet regarding estrogen and cholesterol may misleadingly imply that there is proven benefit of Premarin in regard to risk of coronary heart disease."[174] In March 1995 the Division of Drug Marketing, Advertising, and Communications (DDMAC) at the FDA provided a long letter of revisions to proposed launch materials specifically, the patient care brochure "Hormone Replacement Therapy and Your Health." It included the following noteworthy comment, "DDMAC suggests revising this section [A Commitment to Your Future] . . . DDMAC suggests deleting the last sentence because Prempro is not indicated for all

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[172] W-MDL04782-00141574.
[173] W-MDL04782-00141574.
[174] ROSSC005-000092.

women."[175] Despite this admonishment, Wyeth-Ayerst's efforts to promote hormone supplementation to all menopausal women only intensified in the ensuing years.

In May 1998, Wyeth-Ayerst was instructed by the DDMAC to cease airing the Premarin TV advertisement immediately, "because it is misleading in that it provides an inadequate presentation of the risk information."[176] The communication also noted that, once again, Wyeth-Ayerst's promotion of the benefits of Premarin implied "broader use for Premarin than what appears in the package insert."[177,178] Early the next year DDMAC responded to Wyeth's request for a meeting to discuss lipid claims. The DDMAC noted that Wyeth had failed to address new information available and that, "Unless Wyeth considers this concern and is prepared to discuss its effect on promotion, claims that relate or imply a favorable . . . effect of Prempro on lipid changes may be considered false or misleading."[179]

Following this Agency letter, Wyeth met with officials at the FDA and reviewed the HERS data and Wyeth's insidious marketing techniques. In the Meeting's minutes of February 22, 1999, the FDA's instructions could not be any clearer, "Until further notice, promotional materials should not contain any claims regarding lipid or cardiovascular benefits."[180] Despite repeated FDA admonitions, purported cardiovascular benefit and therapy for all menopausal women continued to be used as marketing tools. Despite the good advice of Wyeth's marketing partner, Ketchum to "Report the Science, Not the Possibilities" and "Don't Suggest Broader Patient Population," [181] Wyeth continued to look for ways to avoid principles of sound and responsible advertising and marketing.

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[175] ROSSC006-001408.
[176] W-MDL04782-00095370.
[177] W-MDL04782-00095371.
[178] W-MDL04782-00095382.
[179] W-MDL04782-00039730.
[180] DUROJ015-000540
[181] HENRL008-000300 at page 0306.

underlying physiologic process being targeted. When targeting for intervention anyone other than those at highest risk, the number of patients needed to treat rises substantially. In the face of these diminishing returns, the impact of adverse events climbs steadily. This was first elegantly described in a seminal article written by Geoffrey Rose and published in the *International Journal of Epidemiology* in 1985.[195] As Douglas Weed subsequently wrote, "[Rose's] ideas have served us well and will continue to do so long into the future."[196]

The core concept that Rose put forward was that there are two types of primary prevention of disease. The first preventive strategy seeks to identify high-risk susceptible individuals and to offer them some individual protection. In contrast, the 'population strategy' seeks to control the determinants of incidence of disease in the population as a whole. Rose noted, "the 'high-risk' strategy seeks to achieve something like a truncation of the risk distribution." Its advantages include that the intervention (e.g. hormone supplementation) is appropriate to the individual and the benefit to risk ratio is favorable. As an example, we do not advise all patients to take cholesterol medication without first testing cholesterol levels.

The 'population strategy' involves mass control methods. Rose writes:

> In mass prevention each individual has usually only a small expectation of benefit, and this small benefit can easily be outweighed by a small risk. Such low-order risks, which can be vitally important to the balance sheet of mass preventive plans, may be hard or impossible to detect. This makes it important to distinguish two approaches. The first is the restoration of biological normality by the removal of an abnormal exposure (e.g. stopping smoking); here there can be some presumption of safety. This is not true for the other kind of preventive approach, which leaves intact the underlying causes of incidence and seeks instead to

[195] Rose G. *Sick individuals and sick populations.* Int J Epidemiol 2001;14:32-38. That the journal republished this article in 2001 with invited commentary is testimony to the critical influence and importance the Rose's paper had on the public health community.
[196] Weed DL. *Commentary: A radical future for pubic health.* Int J Epidemiol 2001;30:440-1.

> interpose some new supposedly protective intervention (e.g. drugs). Here the onus is on the activists to produce adequate evidence of safety.[197]

That is, the bar is higher when demonstrating benefits for an intervention focusing on a population strategy of prevention. Wyeth-Ayerst did not clear this bar prior to selling hormone supplementation as the panacea to the real and perceived ills of menopause. Long-term hormone supplementation should have been reserved for those at highest risk of the single best supported use of the drug treatment – advanced osteopenia with other associated risk factors for fracture or established osteoporosis – until the industry or the government produced adequate evidence of safety from large scale randomized controlled trials. Instead, Wyeth's promotional campaign, as described below, increasingly focused on a population strategy of primary prevention targeting all menopausal women.

Detailed Chronological Summary of Promotional Campaign

Promotional campaign through the 1970's – Menopause is a disease.

Internal Wyeth-Ayerst documents highlight that the promotional machine was put in gear beginning in the 1950's. Beginning a long-standing malapropism where promotion is labeled "education", the company instituted, "a massive program to educate physicians and patients about menopause, vasomotor symptoms, atrophic vaginitis, and the use of Premarin."[198] The company's goal was to foster a, "new understanding of the menopause".[199] The understanding was predicated on the idea that menopause was a deficient state for which the medical establishment had discovered a cure – "replace the missing estrogen".[200] As described above, the book *Feminine Forever* further advanced the medicalization of menopause by describing it as the

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[197] Rose G, op cite.
[198] BURRG002-000050 ("History of Premarin" 10/31/94). The tone of documents describing this early campaign reflects the decidedly paternalistic stand the company took – the marketing campaign presumed women had no knowledge of menopause and needed "education" about a biological event that has been part of the female experience forever.
[199] YAVUE006-001704 (Premarin Family Training Program 1995).
[200] Ibid.

"horror of living decay". Thus, as described in a Wyeth-Ayerst training document, at the beginning of the 1970's the Premarin family was, "poised for unsurpassed new prescriptions and sales volume."[201]

Representative advertisements from 1970 used unfounded statements to change general attitudes about menopause and to make hormone supplementation acceptable and even necessary.[202] These advertisements directed at physicians played on the profession's integrity and pride to not miss the diagnosis of "underlying estrogen deficiency" by attributing symptoms of nervousness, headaches, or sleep disturbance to anxiety and mistakenly administer "a mild sedative or tranquilizer".[203] The ads advised physicians that "to distinguish those [emotional] symptoms that will respond to estrogen replacement therapy from those that may require other approaches to treatment, institute a *therapeutic trial* with Premarin."[204] Note that the recommendation is to begin with a trial of Premarin rather than vice versa.

By 1972, Ayerst advanced the concept of menopause as a disease by equating it with the insulin deficiency disease of type I diabetes mellitus claiming erroneously, in my opinion as an expert clinician who treats both post-menopausal patients and patients with diabetes, that, "It makes as little sense for a menopausal woman to suffer the effects of her estrogen deficiency as it does for diabetic to suffer from his hormone deficiency."[205] The campaign goes on to suggest that when emotional distress stems from loss of estrogen, as in menopause, there is Premarin. And presumably because the ovaries will not resume making estrogen after menopause, despite the lack of long-term studies, for the first time as seen in Contemporary OB/GYN in July 1973,

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[201] RYANJ002-000475 at 000501.
[202] W-MDL04782-00064017. Hormone supplementation will help with the physical symptoms of menopause, primarily hot flashes, but it is erroneous to claim that sex hormones are essential for physical well-being. See also W-MDL04782-00064019, 20, 21, 22.
[203] W-MDL04782-00064019 (8/75).
[204] W-MDL04782-00064021 (8/75).
[205] RYANJ002-000473 (undated).

Meeting,[303] and a comprehensive 49 page Medical Education and Communications Plan.[304] The goal of the National Consensus Meeting was, "to overcome physician/patient misunderstandings in the management of patients suffering from the complications of menopause."[305] DesignWrite anticipated convening multidisciplinary experts, to among other things, "define the serious nature of menopause-related illness . . . and recommend regimens and duration of therapy associated with HRT."[306] The meeting would realize the following marketing objectives: 1) establish a greater need among primary care physicians to treat non-hysterectomized, post-menopausal patients with hormone replacement therapy; 2) overcome the lingering doubts associated with using hormone replacement therapy in post-menopausal patients; 3) develop a strong core of peer-sanctioned scientific information that can be disseminated to physicians, pharmacists and other healthcare personnel through promotion.[307]

The objectives of the Speaker's Bureau Meeting included developing a core national speaker faculty that will influence primary care physicians to institute hormone supplementation more often and earlier.[308] The objectives also included integrating marketing positioning and message strategy into speakers' bureau educational content and materials[309] in a program that amounted to deception – that is, planted positive messages from Wyeth-Ayerst about the benefits of prescribing the Premarin family. The program also sought to build and maintain rapport with physicians who have the ability to positively influence the sales of Premarin.[310] Participants in

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[303] DWRITE 065814.
[304] DWRITE 065764.
[305] DWRITE 065826. It is important to mention that only a small percentage of women ever "suffer from the complications of menopause."
[306] Ibid.
[307] Ibid. Note that this peer-sanctioned scientific information would rely on hand selected multidisciplinary experts who had a favorable view toward menopausal hormone supplementation.
[308] DWRITE 065816.
[309] Ibid.
[310] Ibid.

the Speaker's Bureau meeting included eight to ten faculty members and about 300 physicians already identified from Wyeth-Ayerst's current speaker list.

The stated goals of the Medical Education and Communications Plan included the integration of medical and scientific knowledge of a multi-component, multi-faceted communications and education program. This goal would be accomplished by developing a journal publication plan wherein DesignWrite would write articles favorable to the Premarin family and then see to it that those articles, using the names of recruited "authors" (not the medical writers), got published. Specifically, "content for the publication plan would consist of a mix of peer-reviewed primary research articles, opinion leader-endorsed review articles, journal supplements, letters to the editor, and scientific poster sessions."

According to Jeff Solomon of Wyeth marketing, "One of the rationales for the publication program was the recognition of high clinician reliance on medical articles or journal articles for credible product information. . ."[311] He testified further that Wyeth would create the outline for the expert as a "starting point for a review article."[312] DesignWrite thanked Jeff Solomon for awarding it the Publication Plan "in support of the brand and in defense of the Raloxifene competitive threat..."[313]

DesignWrite assisted Wyeth-Ayerst in controlling and influencing the published scientific information about hormone supplementation that most clinicians ultimately relied on to make their best possible decisions. Controlling this information such that it was favorable to the Premarin family and menopausal hormone supplementation in general would prime health care providers to be receptive to the demand generated by patients influenced by the company's DTC marketing schemes. To execute the publication plan, DesignWrite, working closely with Wyeth-

[311] J. Solomon Deposition at 355-56
[312] J. Solomon Deposition at 317-318.
[313] DWRITE 065950

aging.[409] Notably, while Wyeth had apparently become enamored with promoting hormone supplementation as "a hormonal fountain of youth" just as it had been promoted in the 1960s, medical science was moving forward.

Significantly, in the face of further damaging information regarding the risk of breast cancer with combined hormone supplementation, Wyeth set forth in a "Justification Document" the rationale for changing the breast cancer warning on labeling but remarked that definitive conclusions cannot be stated without randomized, controlled clinical trials.[410] That Wyeth now turned to evidence-based medicine further flew in the face of Wyeth's previous reliance on, "the heritage/trust and confidence of a product that has been used for 60 years . . . can infer an implied "safer" drug in a category where patients are fearful of future cancer risks."[411]

The remainder of 2001 and 2002 up until the publication of WHI (at which time the company was finally forced to rethink and review the science on which their promotional schemes had rested) mimicked the intense marketing efforts of the previous years. DesignWrite highlighted Premarin family 2001 accomplishments.[412] Activities included taking advantage of established relationships with opinion leaders favorable to Wyeth and managing these relationships with the assistance of the marketing agency Ketchum.[413] Additional promotional activities included Wyeth's participation in a patient adherence program,[414] ongoing direct funding of more than 20 studies many of them conducted to delineate additional estrogen

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[409] DWRITE 066317.
[410] ZUCAV008-005665
[411] PANAA004-000607.
[412] DWRITE 026892. Accomplishments included 16 articles, 20 abstracts/posters, breast health and sexuality expert forums, breast health supplement, 3 national symposia, 15th annual estrogen deprivation meeting, slide kits, and sales force support.
[413] See DEVAN001-000350 and CONTA020-000012. The first is a letter written to Reuters Health from Dr. Michelle Warren and faxed by Ketchum explaining that the benefits of HRT have been proven in 60 years of continued use. The second is a letter written to *Harvard Women's Health Watch* from Dr. William Andrews and also faxed by Ketchum explaining that competing hormone replacement therapies do not have an osteoporosis indication.
[414] SOLOJ012-001132.

benefits,[415,416] continued DTCA, Internet initiatives at CBS Healthwatch and RealAge.com, medical education mostly through the National Hormone Council, sales force promotion, providing samples, and the purchase of small gifts for physicians such as "sticky pads".[417,418] The anticipated marketing budget in 2002 was $174,322,000 -- a 37% increase over 2001.[419]

The development of the National Hormone Council – eventually the Council on Hormone Education – with the assistance of DesignWrite deserves special mention. Wyeth sought to position the Council as "**the** [their emphasis] source for information on menopause and HRT."[420] The mission of the council was "advocating for HRT as essential therapy for postmenopausal women."[421] Selected national, and eventually international, opinion leaders would be compensated for time and effort participating in Steering Committee and Working Group meetings, delivering *Distinguished Professor* visits, and attending and presenting at *New Science* meetings.[422]

In short, supported by $10,000,000 from Wyeth,[423] the carefully selected Executive Committee of The Council worked to exert profound control over the dissemination of the entire body of medical and scientific literature regarding menopausal hormone supplementation. Further development saw additional planned activities including "Scientific Update on HRT" slide kits, further distinguished professor visits, a *Journal of the Council on Hormone Education*, a Council on Hormone Education website, reactive public relations activities, proactive public

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[415] SOLOJ007-000053. Studies of additional estrogen benefits including: *Postmenopausal Therapy and Macular Degeneration, HRT and Risk of Uterine Fibroid Growth, Mechanism of Muscle Protein Loss in Menopause,* and *HRT for Prevention of Visceral Obesity in Postmenopausal Women.*
[416] DUROJ012-001110. Wyeth was providing direct funding for at least 5 epidemiologic studies.
[417] LAWT021-009874 at page 9907.
[418] HOLSN016-002298. Invoice for the purchase of $285,974.25 sticky pads printed with "Prempro".
[419] LAWT021-009874 at page 9911.
[420] DWRITE 026976.
[421] DWRITE 026976.
[422] DWRITE 027126.
[423] DWRITE 027055.

relations activities, journal articles in peer-reviewed publications with ongoing assistance from DesignWrite, and symposia.[424] Published science in 2002 including WHI results tested the reactive public relations activities of the council.[425]

Summary of promotional efforts by Wyeth and resulting growth in the Premarin family.

Wyeth's promotional campaign began in the 1950's. It accelerated through the 1960's and early 1970's focusing on redefining menopause as a disease. By 1975, gross annual sales of the Premarin family totaled nearly $60 million.[426] Published scientific evidence linking endometrial cancer to menopausal hormone supplementation prompted the company not so much to re-examine the science of hormone supplementation but to re-examine the marketing strategy. Relying more on these marketing skills (and a growing marketing budget) than science, the company developed a blueprint for marketing that sought to minimize the risks, expand the benefits, and focus on long-term use of hormone supplementation. Using this blueprint, the company reinvigorated Premarin franchise sales. By 1985, gross sales of the Premarin family totaled nearly $82 million annually.[427]

Through the end of the 1980s, by exaggerating the gravity of osteoporosis, Wyeth sought to create fear that would drive otherwise healthy, asymptomatic women to physicians to request hormone supplementation. As discussed above, fear – fear of disease, in particular – undermines autonomy and is a strong driver of behavior. Primed by increasingly intense efforts on the part of Wyeth to manufacture clinical data and scientific opinion, physicians responded to women's

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[424] DWRITE 027078.
[425] CONTA025-02638. An e-mail with the subject line "The Empire Strikes Back" called for identifying 5 or 6 people from the council to serve as coauthors and signatories for a letter to *JAMA* rebutting the unfavorable press regarding HRT.
[426] LAWT006-000913.
[427] LAWT006-000913.

requests for hormone supplementation. By 1990, gross sales of the Premarin family totaled nearly $324 million annually.[428]

Confident about the marketing potential of the Premarin family in the 1990s because of the rapidly expanding menopausal population, Wyeth-Ayerst ignored sound epidemiologic principles and focused on selling hormone supplementation to all menopausal women as a general preventative treatment for long-term use. Wyeth promoted the off-label use of hormones for cardiovascular prevention. In addition, having discovered the power of DTC marketing, Wyeth successfully drove low-risk women to their physicians. By 1995, gross sales of the Premarin family totaled nearly $816 million annually.[429]

Over the next 7 years, in part driven by growing competition from appropriate therapeutic alternatives, Wyeth successfully consolidated its hold on the hormone supplementation market by expanding the marketing campaign on all fronts, utilizing the full catalog of promotional activities,[430] particularly DTCA;[431] and intensifying control over the medical and scientific literature. Wyeth had achieved over 90% market share. In 2001, more than 11 million women in the United States alone used a Premarin family product.[432] Relying on marketing more than science, by 2001, gross sales of the Premarin family surpassed $2 billion annually.[433]

Conclusion

Do the benefits of an integrated promotional campaign outweigh the danger that consumers will demand and take medicines inappropriately?

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[428] LAWT006-000913.
[429] LAWT006-000913.
[430] PANAA001-000019. In 2001, over $1 million for CME, over $3 million in targeted educational grants, over $10 million supporting visiting professor programs.
[431] SOLOJ010-001251. By 2000, the Premarin family was responsible for 82% of total DTC promotional spending in the hormone supplementation category.
[432] W_ANNREP01-0012.
[433] LAWT006-000913.

To reiterate, three factors determine the health impact of promotional campaigns for any given drug: 1) the current prevalence of under-treatment; 2) the amount of inappropriate prescribing stimulated by promotional efforts; and 3) the degree of harm accruing to under-treated compared with over-treated patients.[434] For menopause, it is improbable that there was undertreatment, a large amount of inappropriate prescribing for prevention of disease was stimulated specifically by Wyeth's promotional efforts, and the harm accruing to over-treated patients was substantial.

This balance was tipped decidedly toward cumulative harm by a promotional "crusade" that irresponsibly provided misleading, unbalanced, and "pseudo-educational" information, utilized the full catalog of promotional activities including such deceptive activities as "ghost-writing" and targeted, inappropriately, women unlikely to realize at an individual level important benefits. Furthermore, Wyeth's promotional effort focusing on long-term treatment resulted in presumably millions of women exposed to a medication whose harms emerged after long induction periods. Wyeth undertook this as a "crusade" hammering home the theme "Get Her On, Keep Her On".[435]

Wyeth's promotional efforts occurred decades prior to an adequately completed research agenda. As the esteemed epidemiologist David Sackett writes, "But surely the fundamental promise we make when we actively solicit individuals and exhort them to accept preventive interventions must be that, on average, they will be the better for it. Accordingly, the *presumption* that justifies the *aggressive assertiveness* with which we go after the unsuspecting healthy must be based on the highest level of randomized evidence that our preventive maneuver

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[434] Hollon MF. *Direct-to-consumer marketing of prescription drugs: A current perspective for neurologists and psychiatrists*, CNS Drugs 2004;18(2):69-77.
[435] Contemporary OB/GYN Vol. 1 No. 3, March 1973 and Vol. 2 No 1 July 1973.

will, in fact, do more good than harm."[436] Wyeth did not wait for this randomized evidence that eventually emerged from WHI before pushing a known carcinogen to millions of women.

Returning to epidemiology, Rose posed a question that is an integral part of good doctoring, "Why did this happen and could it have been prevented?"

What were the factors that led to such a rapid and dramatic growth in the number of women taking hormone supplementation? When the activities of many individuals within a group change, it is likely that social facts play a role.[437] The question of why the proportion of women taking hormone supplementation increased dramatically points to potent group-level influences, specifically Wyeth-Ayerst's promotional efforts, that impacted the decisions women and their physicians made together.

Wyeth's sophisticated understanding of marketing and advertising, culminating in an overly aggressive promotional campaign encouraging over-ambitious and unnecessary efforts to prevent osteoporosis as well as unsubstantiated, presumptive cardiovascular benefit drove overuse of long-term hormone therapy in menopausal women. Promotional campaigns drove perimenopausal women with no or few symptoms to seek therapy that promised well-being while campaigns creating fear of osteoporosis and heart disease kept these women on the medications for lengths of time that had never been determined to be safe.

In summary, Wyeth provided "pseudo-educational" information while targeting patients at low risk of fracture and thus, unlikely to realize the benefits of osteoporosis prevention with hormone supplementation. Their efforts tipped the equilibrium decidedly toward net harm caused by the promotional campaign for a carcinogenic drug used to treat a condition that was not under-treated, for which there was ultimately inappropriate prescribing stimulated by the

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[436] Sacket DL. *The arrogance of preventive medicine.* CMAJ 2002;167(4):363-4.
[437] Ebrahim S, Lau E. *Commentary: Sick populations and sick individuals.* International Journal of Epidemiology. 2001;30:433-34.

promotional efforts and the harm accruing to the over-treated patients in the form of breast cancer was substantially greater than the harm accruing to under-treated patients. This is particularly true in light of new developments in osteoporosis therapy.

In conclusion, many women who did not need hormone replacement were driven to seek prescriptions from health care providers who had been primed to respond to this consumer demand, and many women who needed it perhaps only for short-term relief were kept on it for years. Had the campaign emphasizing hormone therapy as the panacea for menopause and emphasizing long-term use not happened, physicians would not have been conditioned to prescribe this drug and most of these women would not have sought out this drug and many women would have avoided the harms attendant to hormone therapy, particularly combination hormone therapy.

To reiterate my opinions set forth above:

1. Wyeth, conducted "a crusade more than a typical pharmaceutical effort."[438]
2. Wyeth accomplished this by expert marketing relying on expanding the perception that hormone therapy is appropriate for every menopausal woman and using aggressive integrated marking tactics targeting physicians and patients together as the "consumer".
3. Wyeth persuaded the medical community and the public that healthy, asymptomatic menopausal women should take hormones for an ever expanding list of symptoms by manufacturing data, purchasing professional opinions, and utilizing the entire catalog of possible promotional activities based on often misleading and unbalanced marketing schemes.
4. Wyeth inappropriately initiated and continued over several decades a "start her on, keep her on" marketing strategy without scientific support for long-term use eventually ignoring sound epidemiologic principles by unreasonably pushing hormone supplementation for population prevention.
5. Wyeth systematically ignored or minimized unfavorable scientific evidence and, thus, failed to adequately warn physicians and patients of the risks of hormone supplementation.

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[438] 4/4 10AM. Bob Essner. Day 3 Close. Plaintiff's exhibit 40.

6. Wyeth eroded the traditional role of the physician as a "learned intermediary" by marketing efforts that knew "no boundaries, no limits."[139]
7. Wyeth nearly seamlessly, from a historical perspective, transitioned women from an early strategy of unopposed estrogen to combination HRT.
8. Wyeth should have reserved hormone supplementation for short-term use and a limited population of consumers, tailoring their marketing campaign accordingly.

All of my opinions expressed in this report are given to a reasonable degree of professional certainty. I reserve the right to supplement my opinions with additional information as it is reviewed or received.

Matthew F. Hollon, M.D., MPH (Date)

2/15/06

[139] 4/4 10AM. Bob Essner. Day 3 Close. Plaintiff's exhibit 40.

EXHIBIT 9

IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF ARKANSAS
WESTERN DIVISION

IN RE: PREMPRO PRODUCTS LIABILITY LITIGATION	: MDL DOCKET NO. : 4:03CV1507 WRW

IN THE COURT OF COMMON PLEAS
PHILADELPHIA COUNTY, PENNSYLVANIA

IN RE: HORMONE THERAPY LITIGATION	: NOVEMBER TERM : 2003 : NO.

CROSS NOTICED IN VARIOUS OTHER ACTIONS

- - -

C O N F I D E N T I A L
SUBJECT TO PROTECTIVE ORDER

- - -

March 27, 2006

- - -

Videotape deposition of MATTHEW F. HOLLON, M.D., held at The Watertown Hotel, 4242 Roosevelt Way NE, Seattle, Washington, commencing at 8:38 a.m., on the above date, before Cindy M. Koch, a Registered Professional Reporter and Certified Court Reporter.

GOLKOW LITIGATION TECHNOLOGIES

Four Penn Center

1600 John F. Kennedy Boulevard

Suite 1210

Philadelphia, Pennsylvania 19103

877.DEPS.USA

CONFIDENTIAL - SUBJECT TO PROTECTIVE ORDER

APPEARANCES:

Counsel for the Plaintiffs
JANET, JENNER & SUGGS, LLC
BY: ROBERT K. JENNER, ESQUIRE
Suite 320, Woodholme Center
1829 Reisterstown Road
Baltimore, Maryland 21208
(410) 653-3200

CLARK, THOMAS & WINTERS
BY: RANDALL L. CHRISTIAN, ESQUIRE
and
SHAVONNE HENDERSON, ESQUIRE
300 West Sixth Street
Suite 1500
Austin, Texas 78701
(512) 472-8800
Counsel for Wyeth

WILLIAMS & CONNOLLY, LLP
BY: JOHN W. VARDAMAN, ESQUIRE
725 Twelfth Street, N.W.
Washington, D.C. 20005
(202) 434-5081
Counsel for Wyeth

ULMER BERNE, LLP
BY: TRACI L. WALLACE, ESQUIRE
600 Vine Street
Suite 2800
Cincinnati, Ohio 45202-2409
(513) 698-5000
Counsel for Barr Laboratories, Inc., Barr Research, Inc. and Duramed Pharmaceuticals, Inc.

SIDLEY AUSTIN, LLP
BY: DEBRA E. POLE, ESQUIRE
555 West Fifth Street
Suite 4000
Los Angeles, CA 90013
(213) 896-6623
Counsel for Pfizer, Inc. and Pharmacia & Upjohn

CONFIDENTIAL - SUBJECT TO PROTECTIVE ORDER

APPEARANCES: (CONTINUED)

DINSMORE & SHOHL, LLP
BY: GABRIELLE M. HILS, ESQUIRE
1900 Chemed Center
255 East Fifth Street
Cincinnati, Ohio 45202
(513) 977-8200
Counsel for Aventis Pharmaceuticals and Watson Laboratories

BAKER STERCHI COWDEN & RICE, LLC
BY: PAUL S. PENTICUFF
500 Crown Center
2400 Pershing Road
Kansas City, Missouri 64108-2533
(816) 471-2121
Counsel for Novo Nordisk Pharmaceuticals, Inc.

SEDGWICK, DETERT, MORAN & ARNOLD, LLP
BY: DAWN SHAWGER
1717 Main Street
Suite 5400
Dallas, Texas 75201-7367
(469) 227-8200
Counsel for Bristol-Myers Squibb

Also present: Ed Burke, Videographer

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By Mr. Christian	10

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THE VIDEOGRAPHER: We are now on the record. My name is Ed Burke, videographer for Byers & Anderson, Court Reporters & Video. We are located at 600 University Street, Suite 2300, Seattle, Washington 98101. Our telephone number is 1 (800) 649-2034.

Today is March 27th, 2006, and the time is now 8:38 a.m. This is the videotaped deposition of Matthew Hollon, M.D., being taken on behalf of the defense in the case of In Re: Prempro Products Liability Litigation, and the MDL docket number for that is 4:03CV1507 WRW. Also in the Court of Common Pleas, Philadelphia County, In Re: Hormone Therapy Case.

This deposition is being held at the Watertown Hotel at 4242 Roosevelt Way Northeast, Seattle, Washington. And will the attorneys please introduce themselves for the record. We'll start on my right and work around.

MR. JENNER: My name is Robert Jenner. I represent the plaintiffs.

MS. WALLACE: Tracy Wallace, for Barr.

MR. PENTICUFF: Paul Penticuff, for Novo Nordisk.

MS. POLE: Debra Pole, for Pfizer and Pharmacia and Upjohn.

MS. HENDERSON: Shavonne Henderson, for Wyeth.

MR. CHRISTIAN: Randall Christian, for Wyeth.

THE VIDEOGRAPHER: The court reporter today is Cindy Koch. Please swear in the witness and proceed with the deposition.

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MATTHEW F. HOLLON, M.D., after having been duly sworn, was examined and testified as follows:

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intentions about anything. If I'm asked to appear in trial to present a best professional opinion, I presume that I'm obligated to do so, but I have no particular intentions of anything along those lines.

Q. But no discussion with you and any of the counsel for Plaintiffs about testifying at trial?

A. Well, I would -- with respect to trying to, you know, get my schedule in place, which I have to do months and months out because I have all these different facets to my job, I have gotten a general sense about what the expectations of my time would be.

You know, family vacation in -- in the summer and things like that, and so I did ask, above and beyond preparing this comprehensive summary of my expert opinion, what the time commitments would be subsequent to that. And I was alerted to the possibility that there would be these upcoming trials in various portions of the country at

various times.

So I'm aware that it's a possibility that I would be asked to testify in the trials in Little Rock, I think as you said, and in Pennsylvania, but -- but I wouldn't say it's my intention at this point in time. Intention doesn't represent --

Q. You haven't made any --

A. Plane reservations?

Q. -- efforts to -- yeah, or marked anything off on your calendar for any particular dates?

A. I haven't been able to at this point in time because I haven't been given any specific dates. Although if there are dates that I need to know about, I should know about them soon because it's -- like I said, juggling all the different responsibilities within my job, the teaching responsibilities and the clinical care responsibilities and my ongoing writing responsibilities, I really need to know about those things far in advance.

Q. Okay. So you reviewed the documents we've identified so far today, and written your report in this case.

Did you do any type of specific study relating to your opinions in this case?

A. Again -- the answer to that is yes, although it's been some time.

Q. Oh, the study that's been published about osteoporosis and the impact of DTC?

A. Yes.

Q. What about with respect to -- since you were retained in this case and reviewed the materials that you reviewed in this case, including the literature and the materials produced by Wyeth, have you done a specific study relating to the stuff you reviewed?

A. Well, my study has involved the skill set that I initially learned pursuing a master's in public health degree, and that's a study of -- that is best summarized in terms of the techniques we use in evidence-based

medicine, and those are question framing.

In this case it's more a question of, How did this happen that -- that -- that Premarin became a $2 billion a year commodity? How did this happen that this prescription drug was promoted to all menopausal women, when their chance of realizing the benefit of the prescription drug was going to be really, really, really tiny, and on balance the potential risks of that medication were likely to outweigh that benefit.

Q. Did you do any --

THE VIDEOGRAPHER: One second. Can we take a five-second break for the tape real quick? One second.

Going off record. The time is 9:38.

Okay. Just give me five seconds. We'll come right back up. We are back on record. The time is 9:38.

Q. (By Mr. Christian) Did you do any surveys of physicians or of

patients relating to your work in this particular case?
A. Well, I -- a survey is kind of a limited instrument in terms of providing a --
Q. I'm just asking if you did it or not.
A. Well, I'm trying to answer your question.
Q. Well, did you do a survey or not, related to your opinions in this case?
A. Well, it's a limited utility in terms of answering the questions that were posed to me, and thus it wouldn't be helpful in -- nor would I have had time.
Surveys take extended periods of time to craft. You have to get human subjects' approval, which can take months and months and months, so it would have been unrealistic for me to conduct a survey related to the opinions that I render in a case.
MR. CHRISTIAN: Objection.

Nonresponsive.
Q. (By Mr. Christian) My question is, did you do a survey related to your opinions in this case?
A. I'll just repeat the answer that I provided to you, which was --
Q. I've already heard that answer. I need to know -- answer whether you actually did one or not.
MR. JENNER: He answered the question, Counsel.
MR. CHRISTIAN: No, he didn't. He said --
Q. (By Mr. Christian) Did you do a survey?
A. Within the -- I'll answer it again. The -- my responsibility, as an expert in this case, is to look at the universe of -- of available facts that I have here, and use the skill set --
Q. Can you answer the question? Did you do a survey in the case?
MR. JENNER: Objection.
Q. (By Mr. Christian) Did you

do a survey?
MR. JENNER: Asked and answered.
A. To use the skill set that I have --
Q. (By Mr. Christian) I'm not asking you that question. Did you do a survey?
A. To use the skill set that I have to --
Q. Can you not answer that question, Dr. Hollon?
MR. JENNER: Tell you what, let's start -- let's ask him a new question. We'll start all over.
Q. (By Mr. Christian) All right. It's true, is it not, Doctor, that you have not conducted a survey with respect to your opinions in this particular case?
A. I have not conducted a survey.
Q. Okay. And you have not conducted any focus groups with respect to your opinions in this particular case,

correct?
A. Focus groups, again, would take -- it wouldn't be useful to this case.
MR. CHRISTIAN: Objection. Nonresponsive.
Q. (By Mr. Christian) Did you do a focus group with respect to your opinions in this case? Yes or no? Did you do one?
A. The answer is the same I would provide. If I thought that a focus group --
Q. Did you do one, Dr. Hollon?
A. If I thought that a focus group was going to be helpful --
Q. I'm not asking you whether you thought about it or not.
MR. CHRISTIAN: Objection. Nonresponsive.
Q. (By Mr. Christian) Did you do a focus group with respect to your opinions in this case?
MR. JENNER: Dr. Hollon, you can answer it yes or no, and

then give an answer as to what you did, either way.

A. Okay. So I have not conducted a survey because -- I have not conducted a survey and I have not conducted a focus group because the tools or skill set that I would need to arrive at to prepare this report are fundamentally different from -- or were useful in a different way than -- than the -- than the -- than the skill set of a -- or conducting a survey or conducting a focus group.

Didn't have time to do one, and it -- and it didn't directly -- wasn't directly necessary to prepare my professional opinion.

MR. CHRISTIAN: Objection. Nonresponsive, everything from "because" on to the end.

Q. (By Mr. Christian) You're aware, Doctor, that the universe of the Wyeth documents that were sent to you are documents that Plaintiffs' counsel selected from a bigger universe that

Wyeth produced to Plaintiffs in this case? Do you understand that?

MR. JENNER: Objection.

A. Well, the documents that were sent to me were definitely sent by the plaintiffs. I recognize that. I also was sent a hard drive that included documents that weren't there, and I don't know, honestly, if that represents a complete universe or not.

It's my responsibility, as a researcher and scientist, to try and triangulate and to review as much as I can to form an opinion so that my opinion is valid.

And to that extent, as I mentioned before, I tried my best to just randomly select documents from the hard drive that would -- if I could find something that would serve as a counter to the opinions that I form in here, I looked for those documents on the hard drive, and then went back to look in the medical literature, as well, and in the popular literature, using like LexisNexis

databases or things like that.

And surprisingly, I wasn't able to find any compelling documents that would counter the opinions -- the professional opinions that are presented in my report.

MR. CHRISTIAN: Objection. Nonresponsive.

Q. (By Mr. Christian) Did you ever ask the plaintiffs' counsel for additional Wyeth documents, other than the ones that they had sent you?

A. There was one occasion.

Q. Okay. And what was that?

A. The occasion was around sources of money that were being used to fund a study that was going to be favorable to the Premarin family of products. And so I had asked about whether or not there was any documentation -- concrete documentation of Wyeth investing in a study to their favor.

Q. And did you receive a response from Plaintiffs' counsel?

A. Yes.

Q. And is that a document that they responded?

A. It was a document -- if I remember correctly, it was actually a check, or an invoice that showed "paid" or something like that, from Wyeth to the investigators.

Q. And is that reflected in Exhibits 9 and 10?

A. I don't think so because that specific detail in the end did not have direct -- that little piece of the puzzle did not have relevance to my over- -- direct relevance to my overall opinions, and so I don't think I included it in there.

I'm not actually sure where it is in all of that stuff. I wouldn't have printed it out, so I'm not sure it exists anymore.

Q. Okay.

A. Or -- it exists somewhere, but I just don't have it.

Q. Did you review any medical

records of any of the plaintiffs in this case?
A. No.
Q. Did you review any depositions of any of the plaintiffs or any of the doctors taken in this case?
A. Of the plaintiffs or the doctors. Which doctors are you talking about? Like Dr. Sackett, or --
Q. The doctors that prescribed the Premarin or Prempro to the plaintiffs in this case, did you review any of those depositions?
A. No, I did not.
Q. Did you review any summaries of information regarding the plaintiffs in this case, the specific plaintiffs?
A. No. But I don't think that affects my ability to judge the overall impact of marketing or drug promotion of the Premarin family on prescribing --
MR. JENNER: Wait for the next question.
MR. CHRISTIAN: Objection.

Nonresponsive from everything starting with "but."
Q. (By Mr. Christian) We've marked as your report Exhibit No. 4, correct?
A. Yes.
Q. And you prepared this report?
A. I did, yes.
Q. And did you send a draft of it to Mr. Jenner or any other Plaintiffs' counsel before it was completed?
MR. JENNER: Objection. Asked and answered.
A. As mentioned, oh, I don't know actually if we -- I did send drafts.
Q. (By Mr. Christian) Okay. And did you receive any edits or comments by Plaintiffs' counsel regarding your draft report?
A. They weren't edits about content. I was more -- I solicited Mr. Jenner's opinions about structure, but nothing specific about the content in the report. And by "structure," I mean

organizational structure, and then topic areas that were topic areas that needed to be covered.
Q. And does Exhibit 4 fairly and accurately summarize your opinions you intend to offer at trials in this case?
MR. JENNER: Objection.
A. To the extent that I've been able to review documents available to me, it reflects my best professional opinion or best -- yeah, best professional opinion about the facts of Wyeth's overpromotion of Premarin family of products.
Q. (By Mr. Christian) And did you review all the references that are contained in the report?
A. Yes.
Q. Do you strive to be accurate in your characterization of those references?
A. Of course.
Q. You weren't trying to put your spin on any of the documents that

you referred to, were you?
A. No. That's not my responsibility. My responsibility in -- as a physician, as a teacher, as a researcher, is to be as accurate as humanly possible.
Is there a possibility that there are -- I know of one, where there's actually something that -- that's listed without a reference number in it in there, and now I can't remember where it is off the top of my head, but there may be like a missed reference or something.
Q. Did you only try to pull things out of the references that supported the plaintiffs' case?
MR. JENNER: Objection.
A. Oh, absolutely not. As I said to you before, I was skeptical -- I was concerned about that --
Q. (By Mr. Christian) That's -- you've answered my question, Doctor.
A. Okay.
Q. And do you -- I guess you've revised and proofread Exhibit 4?

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teaching evidence-based medicine, although certainly the trend in the country is to teach these skills to students as well as residents, and there is a program at the University of Washington.

Q. On your -- your Web site kind of breaks down the steps in practicing evidence-based medicine, and it says first that, convert the need for information into an answerable question.

Does that sound accurate?

A. Correct.

Q. And then to track down the best evidence for its validity, impact, and applicability.

Does that sound accurate?

A. Uh-huh.

Q. Is that a yes?

A. Sorry. Yes.

Q. And then it -- the next step is to critically appraise the evidence for its validity, impact, and applicability.

A. And that's often the most

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challenging part. So for a lot of the residents, we teach a simple set of rules that aren't as comprehensive as the skills that we learn in the school of public health, as an example.

Q. And are your residents at University of Washington medical school able to -- to learn how to correctly appraise the evidence for its validity, impact, and applicability?

A. Say again?

MR. JENNER: Objection.

Q. (By Mr. Christian) Are you able to teach that to the residents?

A. Say that again?

Q. Are you able to teach your residents to critically appraise the evidence for its validity, impact, and applicability to the patient?

A. Of course.

Q. That's one of the steps, and that's what you're teaching the students, right?

A. Yes. Correct. And they're not students, they're residents. And we

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teach -- that's exactly what we teach them, and we work together closely to acquire those skills as -- as best as they can in the time allotted.

I mean, residents are really busy. You know probably that they, you know, have enormous clinical responsibilities, and generally have 80-hour workweeks, and so this is sandwiched into a small portion of their overall training program.

Q. Then the last step that you list is, integrate the evidence with clinical expertise and your patient's characteristics and values.

Does that sound accurate?

A. Sure. If a patient, for instance, refuses -- well, let's leave it at that.

Q. Okay.

A. That's accurate.

Q. And the patient's characteristics are defined as the unique preference, concerns, and expectations each patient brings to a clinical

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encounter?

Does that sound accurate?

A. Yeah. Yeah. What's amazing now, in nowadays -- these days is to think about all of the --

Q. I was just asking if that's accurate.

A. Yeah. It's great to think about all of the various things that influence. That's partly, like, why I initially got involved in this topic as a fellow, is to stop and -- for a moment and recognize, especially --

Q. Doctor, I'm sorry. We have a limited time period today--

A. No, no, no. This is important.

Q. You're just telling me your personal feelings about why --

A. No, this is professional. Actually, I'm sorry, this isn't personal. This is --

Q. But I didn't ask you that question. I only have a limited amount of time today, and we have 500 references

to go through, and so I need you to answer the question I ask you.
MR. JENNER: Just wait for the next question, Dr. Hollon.
Q. (By Mr. Christian) Now, only a doctor can integrate their clinical expertise with the patient characteristics; is that correct?
MR. JENNER: Objection.
A. Can you rephrase that question?
Q. (By Mr. Christian) Sure. A pharmaceutical company cannot be involved with the patient characteristics, their preferences, concerns, and expectations; is that correct?
MR. JENNER: Objection.
A. That's not correct.
Q. (By Mr. Christian) Of a particular patient that comes in to see a doctor.
A. I think that's -- what you're -- the way you're stating that is inaccurate. Actually, the pharmaceutical

industry has a substantial influence in this day and age, not only on healthcare providers, but they have substantial influence, as is evidenced by the -- all of the documents that I have provided in my report.
They have substantial influence on beliefs and values and choices that the patient provider team makes together.
Q. Okay. Do you have any evidence that Wyeth knows the unique preference, concerns, or expectations of any particular patient that's come in and asked for Premarin or Prempro?
MR. JENNER: Objection.
A. Can you rephrase that question, please?
Q. (By Mr. Christian) Do you have any evidence that Wyeth knows unique preferences, concerns, or expectations of a particular patient that's asked for Premarin and Prempro, to a doctor?
MR. JENNER: Objection.
A. I have a wealth of evidence

that says that Wyeth sought to influence those preferences.
Q. (By Mr. Christian) I'm asking you --
MR. CHRISTIAN: Nonresponsive -- objection. Nonresponsive.
Q. (By Mr. Christian) I'm asking you whether you have any experience for a particular patient?
MR. JENNER: Objection. Asked and answered.
A. I don't have evidence for a particular patient, but what we would say is --
Q. (By Mr. Christian) Okay.
MR. JENNER: Let him finish his answer.
A. -- comprehensively, looking at the big picture of this, is that Premarin family became a $2 billion a year commodity, and it's reasonable -- it's reasonable for all of us to stop and say, Gosh, how did that happen? And what unequivocally --
Q. (By Mr. Christian) Doctor,

you understand I have --
MR. JENNER: Whoa, whoa, whoa, whoa.
Q. (By Mr. Christian) -- the ability to ask questions and ask about your opinions today, right?
A. And in -- my --
Q. And you've mentioned this $2 billion a year about ten times today.
A. Uh-huh.
Q. Okay. Are you going to allow me the opportunity to ask you specific questions, and will you answer -- give me the courtesy of answering my particular questions?
MR. JENNER: Okay. Objection. Hold on. Wait, wait, wait. He's doing his best -- first time deponent, to answer your question the best he can. Why don't you ask your next question, and the doctor will do his best to answer.
Q. (By Mr. Christian) The basics of evidence-based medicines, you

This is the end of Tape No. 1.
(Recess.)
THE VIDEOGRAPHER: We are back on record. The time is 10:52. This is the beginning of Tape No. 2.
Q. (By Mr. Christian) Doctor, are you ready to proceed?
A. Yeah, I'm ready.
Q. Do you know how many meta-analyses were published in the 1990s showing a cardiovascular benefit for women taking hormone therapy?
MR. JENNER: Objection.
A. The shortcomings of those meta-analyses that I think you're referring to --
Q. (By Mr. Christian) Do you know how many? That's my question, is, do you know how many?
A. Well, off the top of my head, without going back and looking, I don't have a sense of how many. But the shortcomings of all of those meta-analyses is that they were based on

observational evidence, which we clearly know has limitations and ought to be recognized in the context of our practices.
Q. And you're not an epidemiologist, are you, Doctor?
A. I'm trained in the skills of epidemiology, and I use those skills that I've been trained in to be an expert in evidence-based medicine.
I'm a -- my -- I have a breadth of expertise across a range of areas that include marketing, or the promotion of prescription drugs, the clinical practice related to osteoporosis and osteoporosis prevention, and then issues of population prevention of conditions.
Q. Do you have any particular critiques of the meta-analyses that were published in the 1990s showing a cardiovascular benefit of women taking hormone therapy?
MR. JENNER: Objection.
A. Which meta-analyses are you

referring to?
Q. (By Mr. Christian) Well, you haven't identified that you even know what they are, so --
MR. JENNER: No, objection. That wasn't the question.
A. That's not true. You asked me how many meta-analyses there were. I can't explain to you how many meta -- I can't tell you how many meta-analyses --
Q. (By Mr. Christian) You don't know?
A. Huh?
Q. You don't know?
A. There were meta-analyses done. It's not a --
Q. You don't know how many, though, right?
A. I don't know how many. I can tell you that there were meta-analyses that were done that were based on observational evidence that has significant limitations, that were eventually demonstrated by subsequent large-scale, randomized control trials

evaluating cardiovascular benefit.
Q. Do you know how many practice guidelines were available in the 1990s revealing a cardiovascular benefit to women taking hormone therapy?
A. Practice guidelines don't reveal anything.
Q. Okay. Do you know how many practice guidelines existed in the 1990s discussing cardiovascular benefit of women taking hormone therapy?
MR. JENNER: Objection.
A. I'm sure there were several.
Q. (By Mr. Christian) Did you go back and look at any of those?
MR. JENNER: Dr. Hollon, give me the opportunity to object, and then you can answer the question.
THE WITNESS: Oh, okay.
MR. JENNER: Objection. Go ahead.
Q. (By Mr. Christian) Did you go back and look at any of those

guidelines from the 1990s before offering your opinions in this case?

MR. JENNER: Objection.

A. I don't recall specifically looking at clinical practice guidelines because, as I said before, clinic -- or tried to say before to you, the clinical practice guidelines generally tend to fall low on the evidence-based medicine period -- pyramid.

They're not necessarily considered best standards of evidence. They can be a -- if they're done right, they can be considered reasonable standards of evidence, but they're not the highest standard of evidence, like a randomized control trial.

Q. (By Mr. Christian) They are in the group that's considered best evidence for evidence-based medicine?

A. They're --

MR. JENNER: Objection.

THE WITNESS: Excuse me.

MR. JENNER: Go ahead.

A. They are considered a

potential source, depending on who does them, how they're conducted. There are evidence-based clinical practice guidelines, and there are some -- also -- you're lumping clinical practice guidelines into this one big category.

And there are certain organizations that conduct evidence-based clinical practice guideline summaries, and there are some that do not tend to use the techniques of evidence-based medicine to generate their clinical practice guidelines.

And those guidelines are oftentimes influenced by, you know, other -- other sources of information than simply best medical literature.

Q. (By Mr. Christian) Can you identify any guideline today that's been influenced by other sources of information for us?

A. Well, I --

MR. JENNER: Objection.

THE WITNESS: Excuse me.

A. Do you have a guideline

that I could review for you?

Q. (By Mr. Christian) I'm just asking if -- if y'all -- as you sit there today, can you name some guidelines that did not use evidence-based medicine, or the best evidence to support their guidelines?

MR. JENNER: Objection.

A. I can't name any specifically for you. But you -- if you want to provide me one -- with one, I'd be happy to look at it.

Q. (By Mr. Christian) You didn't go back and do that for purposes of this case, did you?

A. Look at clinical practice guidelines?

Q. Right.

A. I did not look at clinical practice guidelines because, by and large, they don't represent the highest level of evidence.

Q. Did you go and look at the National Guideline Clearinghouse to see if they had any information about hormone

therapy use?

A. Well, the National Guideline Clearinghouse is just that. It's a clearinghouse for guidelines of all different flavors, and some of those would be evidence-based guidelines and others would be guidelines that don't use the most rigorous methods of evidence-based practice to generate their guidelines.

So a clearinghouse is a good starting place for trying to find guidelines, but it doesn't necessarily tell you whether or not the guideline that you're looking at is -- really represents the highest level of medical evidence.

MR. CHRISTIAN: Objection. Nonresponsive.

Q. (By Mr. Christian) Did you go look at the Cochran database of systematic reviews to see what it had to say about hormone therapy?

A. I've looked at Cochran a lot. I use Cochran frequently. Did I

condition of osteoporosis, as the FDA has said, is undertreated?
MR. JENNER: Objection.
A. I would agree with that, that historically the condition of osteoporosis, so that is the small percent of women who have T scores of minus 2.5 or greater or an established fracture that we -- as a healthcare society, we're not adequately identifying those women and treating those women, but that's changed -- when was that statement made by the FDA?
Q. (By Mr. Christian) It was made in 2004.
A. Yeah. And so that's -- you know, I think that that is changing, and is probably changing as a consequence of that -- in part, the FDA's statement, but a lot of the other factors are influencing how we address the public health problem of osteoporosis, which is --
Q. So when you say it's changing, it's becoming less undertreated

since 2004?
A. Yeah.
Q. Okay.
A. I think it's being less under -- I don't even think since 2004, the last -- really the last five year -- five to ten years the condition of osteoporosis has become less undertreated.
Q. Now then, your second factor, with respect to the doctors who prescribed hormone therapy to the plaintiffs in this case, you cannot say whether or not that prescription was inappropriately stimulated by promotional efforts, can you?
MR. JENNER: Objection to the form.
A. I'm sorry. Rephrase the question.
Q. (By Mr. Christian) With respect to factor number two, you are unable to say in this case whether or not any particular plaintiff in this case inappropriately was prescribed hormone

therapy which was stimulated by promotional efforts?
MR. JENNER: Objection.
A. Actually, I think what we can say is that the sum of the promotional efforts by Wyeth clearly and unequivocally influenced prescribing practices in this country.
Q. (By Mr. Christian) I understand that that's your opinion generally, that it had some influence.
A. Uh-huh.
Q. But with the particular plaintiffs in this case, you cannot say a single one of those plaintiffs in this case was inappropriately prescribed hormone therapy due to stimulation by promotional efforts on behalf of Wyeth, can you?
MR. JENNER: Objection.
A. Well, I haven't met them.
Q. (By Mr. Christian) Okay. So you can't say that, right?
MR. JENNER: Objection.
A. I can't say yes or no.

Q. (By Mr. Christian) Okay. So you can't --
A. I'm not given adequate information at this point to answer your question.
Q. With the information that you have now, you cannot say that any plaintiff in this case was inappropriately prescribed hormone therapy, based upon promotional activities?
MR. JENNER: Objection.
A. I can, I think, with certainty, based on looking at the magnitude of promotional efforts that were put in to getting all women on hormone supplementation, women who had very low risk of ever suffering the consequences of osteoporosis, given the magnitude of promotion, and the fact that by, what, 2001 there were nearly a billion prescriptions of -- in the Premarin family that had been written, that it's more likely than not that there are physicians and patients out there who

were un- -- in- -- unduly influenced by the promotional efforts that subsequently led to this harm.

MR. CHRISTIAN: Objection. Nonresponsive.

Q. (By Mr. Christian) Identify a single plaintiff in this case who was inappropriately prescribed hormone therapy which was stimulated by Wyeth promotional efforts.

A. I haven't --

MR. JENNER: Objection.

THE WITNESS: I'm sorry.

A. I haven't been given the name of the plaintiffs.

Q. (By Mr. Christian) So you cannot do that?

MR. JENNER: Objection.

A. Again, I cannot either do it or not do it. All I can comment on is the extent to which the promotional efforts of -- of Wyeth influenced the prescribing practices, the decisions that patients and physicians made together, about whether or not somebody would get

what ultimately proved to be a carcinogenic substance.

Q. (By Mr. Christian) You have not reviewed any information about the plaintiffs in this case; is that correct?

A. That's correct.

Q. Okay. You don't know why any single plaintiff in this case took hormone therapy, correct? You don't know the reason why they took it?

A. I don't know the reason why a plaintiff took hormone therapy in this case.

Q. You don't know a reason why any of the plaintiffs in this case went to the doctor and was prescribed hormone therapy, do you?

A. I haven't had -- I can't -- again, I don't have the information to answer that question, nor is it really -- would I at this point, I guess, consider -- my responsibility is to use my expertise on -- on marketing promotion, on osteoporosis, and on public

health prevention, which is something that I practice day in and day out. I have discussions about, how can I keep you healthy? How can we keep you vital?

I rely on those expertise to look at this information and -- and come to the conclusion that the comprehensive promotional efforts of Wyeth, these integrated marketing tactics, through all these different channels, are beyond a reasonable doubt to have had influence on prescribing --

Q. Doctor --

MR. JENNER: Just let him finish his answer.

A. -- on prescribing practices in this country.

MR. JENNER: Let him finish his answer.

Q. (By Mr. Christian) You've been repeating the same thing over and over.

MR. JENNER: Because you ask him the question over and over again.

Q. (By Mr. Christian) I understand that you have opinions in this case, and you're going to have ample opportunity to give those opinions, if the Court allows it.

But I'm entitled to ask a question in this case and get an answer to it.

A. Uh-huh.

Q. And the fact is, you don't know whether any of the plaintiffs in this case, what promotional materials they may or may not have seen, do you?

MR. JENNER: Objection.

Q. (By Mr. Christian) In this case, you don't know?

MR. JENNER: Objection.

A. I haven't been provided with that information.

Q. (By Mr. Christian) Okay. Well, that's -- I'm just asking the question --

A. So I can't render an opinion.

Q. So you can say no, I don't

know, right?
A. So I --
Q. I'm not asking for an opinion. I'm asking whether or not you know what promotional pieces, if any, any of the plaintiffs in this case saw.
A. Well, beyond a reasonable doubt I can tell you that given the scope of the marketing program, that most --
Q. Doctor, we have a limited time today, and you know the question -- the answer is, you don't know whether any plaintiff in this case, what piece -- any promotional piece that they saw?
MR. CHRISTIAN: All right. Hold on. Stop.
Q. (By Mr. Christian) You don't know the answer to that question.
MR. JENNER: Stop, stop, stop. We're not going to lose our temper. We're not going to yell at each other. We're going to ask questions. I'm going to object or not object. He's told you what he's reviewed, what he's not

reviewed. He's given his answer. Ask your next question.
Q. (By Mr. Christian) You can't say what any plaintiff in this case saw with respect to Wyeth promotional pieces?
MR. JENNER: Objection. Asked and answered.
A. I can say that based on the scope of the promotional efforts, that more likely than not, okay, for the women in this country, the impact of Wyeth's promotional efforts through all of the various channels that they used, direct-to-physician advertising --
Q. (By Mr. Christian) Let's put it this way --
MR. JENNER: Let him finish, please.
(Unintelligible crosstalk.)
THE COURT REPORTER: I'm sorry; I need for everybody to speak one at a time because we're just getting crosstalk.
Q. (By Mr. Christian) Let me

go about it this way.
MR. JENNER: He's asked -- you've asked him six times whether he's seen the medical records. He's said he hasn't. So I don't know what else you're going to ask him. He's given his answer.
Q. (By Mr. Christian) That answer about whether or not or what a particular plaintiff saw in this case with respect to promotional materials is something that could be answered by reviewing the depositions of the plaintiffs in this case, correct?
MR. JENNER: Objection.
A. It could possibly be answered. Although a lot of times the interesting thing about promotion is that you may not be able to recall all of the things that have influenced you in making a decision about how you prescribe or pursue a specific health issue.
So it may be that they -- that they were influenced by something, but they don't specific -- they aren't

specifically able to identify what that thing was, so it could possibly help.
Q. (By Mr. Christian) You don't know the reasons why any of the prescribing physicians in this doctor -- in this case prescribed hormone therapy to the plaintiffs in this case, right?
MR. JENNER: Objection.
A. Well, again, what I would say there is that what I can -- the only thing -- the only way I can answer that is to say that based on the intensive effort of Wyeth's promotional campaign, that the decisions that physicians and patients made together were unduly influenced by what was an irresponsible campaign that advocated population prevention, okay, a population prevention strategy for women at exceedingly low risk of ever developing the consequences or suffering the consequences of osteoporosis.
Q. (By Mr. Christian) Tell the jury what promotional material Ms. Reeves saw.

MR. JENNER: Objection.
A. I'm not sure that -- where -- which jury?
Q. (By Mr. Christian) The jury that may ultimately see this tape.
A. I don't -- I mean, there's no jury here.
Q. I know, but this tape can be played at trial. Did you -- were you aware of that?
MR. JENNER: Objection.
A. I'm -- again, I -- you know, have -- I'm not, I guess, aware of that.
Q. (By Mr. Christian) Well, just so you're aware, to the extent it's admissible, this videotape may be used at a trial in this case.
A. Uh-huh.
Q. So the jury may be watching this.
A. Uh-huh.
Q. And I want you to tell the jury what promotional piece Mrs. Reeves saw?

MR. JENNER: Objection.
A. I can't tell you what promotional piece Mrs. Reeves saw, but it doesn't --
Q. (By Mr. Christian) Can you tell us --
A. -- I think that doesn't change the fact that what we know, or the facts in this case reveal was that the -- given the extent of the promotional campaign, that it certainly had undue influence on prescribing practices within this country.
MR. CHRISTIAN: Objection. Nonresponsive, starting with the word "but."
Q. (By Mr. Christian) Tell the jury what promotional material Mrs. Rush saw.
MR. JENNER: Objection.
A. Well, again, I can't do that without having reviewed Mrs. Rush's deposition, and then I would still have concerns about whether or not she was able to recall the specific influences

that led her to make the decision they did.
What we know is that Wyeth's influences were pervasive and really sought to be channeled through a comprehensive set of mark- -- or channeled through a comprehensive set of marketing avenues, basically.
MR. CHRISTIAN: Objection. Nonresponsive starting with the word "but."
Q. (By Mr. Christian) What promotional material did Dr. Caldwell see?
MR. JENNER: Objection.
A. Who's Dr. Caldwell?
Q. (By Mr. Christian) You don't know who Dr. Caldwell is?
A. (Witness shakes head.)
Q. He's one of the physicians that prescribed hormone therapy in this case.
A. Uh-huh.
MR. JENNER: Objection.
Q. (By Mr. Christian) Can you

tell us what promotional material Dr. Caldwell saw?
MR. JENNER: Objection.
A. Well, I can't tell you specifically what Dr. Caldwell saw, but based on the nature of the -- of Wyeth's marketing campaign that's outlined in my report here, I'd say beyond a reasonable doubt physicians in this country were unduly influenced by a -- by a promotional campaign that went through a host of different channels.
And what's interesting is that physicians, unfortunately, are notorious at denying the influence of promotional material in their prescribing practices.
So if you stood outside of a hospital and said, Today in your practice, is the person who walked -- every doctor comes and walks in, and you say, Are you going to be -- you know, does -- does the -- having seen a drug rep for am- -- for Norvasc or amlodipine influence your prescription of writing

the prescription for Norvasc, doctors will always say no.

But when you go back and look at the primary literature, it's clear that the increasing number of interactions between healthcare providers or physicians and the pharmaceutical industry unduly influence its prescribing habits, and did so in this case -- in the case -- in the case of hormone supplementation that we're looking at here.

MR. CHRISTIAN: Objection. Nonresponsive, everything after the word "but."

Q. (By Mr. Christian) How was Dr. Caldwell unduly influenced in this case?

MR. JENNER: Objection.

A. Well, I've never met Dr. Caldwell, so all I can speak to is the channels, or the -- the -- the factors that led to a promotional scheme that said all women should be on hormone supplementation, and all women should

continue it for indefinite periods of time, and they should start it as soon as they begin menopause.

And my concern with that is that that's a -- what's called a population prevention strategy. Okay? And when you're talking about -- when you're talking about prescribing a medication --

Q. Doctor, I'm sorry, I -- we've got so much to cover here today.

A. Uh-huh.

Q. All I asked you is, what ads or promotional material did Dr. Frazier see, and you obviously don't know the answer to that question.

A. Caldwell, I thought you asked.

Q. No, I've moved on to Dr. Frazier now.

A. Okay. Uh-huh.

Q. And I really -- you think it's fair for Wyeth to be able to come in and ask you specific questions and get answers to those questions?

MR. JENNER: Objection. You don't need to answer that.

Go on and ask your next question.

Q. (By Mr. Christian) You think that's fair?

MR. JENNER: Objection. Go ahead, ask your next substantive question about his opinions. You don't have to talk to him about legal procedures.

Go ahead.

MR. CHRISTIAN: I'm just talking about fairness.

MR. JENNER: All right. Don't answer the question. Wait until your next question.

Q. (By Mr. Christian) Now then, you also have your third factor is looking at the harm accruing to overtreated patients -- I'm sorry, the degree of harm accruing to undertreated compared with overtreated patients.

Now then, do you agree that

the risk of long-term use of estrogen or hormone therapy are small?

A. One moment. Okay?

MR. JENNER: Objection.

A. It's actually -- just give me one second here. What I want to -- yes, the answer to your question is, small risks are -- can be really, really important.

Q. (By Mr. Christian) Okay. So you agree that the risks are small, but may be important?

MR. JENNER: Objection.

Q. (By Mr. Christian) Is that --

A. The risks are important to -- the risk is not small to the person who develops breast cancer. That risk is real.

The measured estimates of risk overall are not tremendous, but they're important, especially when you look at the balance sheet of risks and benefits.

Q. Let's go back and look at

Exhibit No. 14.
A. Which one is Exhibit 14?
Q. It's the 1999. Do you have that?
A. Yeah.
Q. Exhibit 14?
A. All of my notes here are kind of messed up. I'm going to pause for a moment, if that's okay.
THE WITNESS: Rob, is it appropriate to ask you to put these back --
MR. JENNER: I can do it.
THE WITNESS: -- in page order? Because I've got my pages mixed up.
MR. JENNER: Sure.
A. Okay. I'm ready. Sorry about that.
Q. (By Mr. Christian) Exhibit 14 in front of you, and this, as you characterized yourself, was an opinion piece, right?
MR. JENNER: Objection.
A. As I characterized earlier

today, this is a piece that has opinions within it that are formed on the basis of an assessment of the available, but limited literature on the potential impact of direct-to-consumer marketing of prescription drugs.
Q. (By Mr. Christian) Well, Doctor, if you look at Exhibit No. 11, it's another editorial that you wrote. You say that you published -- you and Dr. -- and Mr. Holmer published paired opinion pieces. That's what you wrote about your 1999 article.
A. So maybe we should -- maybe we can clarify that, that -- and say that maybe what exactly I should have wrote is that we published paired pieces which contained opinions.
Q. Oh, okay. That's what you should have written there?
A. Well, perhaps it more accurately reflects. But I mean, it's also reasonable to summarize that because this piece has opinions in it, it's an opinion piece. But it also contains what

you're ignoring then, is you're ignoring the comprehensive --
Q. Well, I'm not ignoring --
MR. JENNER: Let him finish his answer, please.
A. You're ignoring all of the energy and work that I did into compiling all of the available evidence on direct-to-consumer marketing at that time, which was a huge stack that represented a tremendous amount of work and skills -- expert skills to summarize.
Q. (By Mr. Christian) You wrote Exhibit 11, correct?
A. Yes. I wrote this one, as well.
Q. Exhibit 14, going back to your 1999 article, you did not have much evidence to substantiate your arguments back then, did you?
MR. JENNER: Objection.
A. There -- I -- what do you mean by "much"?
Q. (By Mr. Christian) Well, that's what you wrote.

A. Uh-huh.
Q. What did you mean when you wrote that you didn't have much evidence to substantiate your argument?
MR. JENNER: Objection.
A. What I meant -- that's a good question. What I meant at that point in time is that we didn't have any kind of reasonable -- because direct-to-consumer marketing was relatively new, we didn't have -- not that this couldn't conceivably be done, but we didn't have like a large randomized trial.
So the professional opinions that I eventually render in the 1999 article are based on what evidence I could gather. Some of that evidence looked at direct-to-physician advertising and the potential impacts and content of direct-to-physician advertising, and then there was some limited data, including some data on stuff that wasn't in peer reviews on the potential impact of direct-to-consumer marketing, like the Consumer Reports publication.

Q. Is that something you'd go back and revise now, your statement that you did not have much evidence to substantiate your arguments?

MR. JENNER: Objection.

A. I'm sorry. Say that again.

Q. (By Mr. Christian) You're the one that wrote that -- your 1999 article, you did not have much evidence to substantiate your arguments?

A. You're referring to what's written in this one?

Q. Right. Would that be something you'd want to revise today, to --

MR. JENNER: Objection.

Q. (By Mr. Christian) -- change that language?

A. Change it to what?

Q. You're the one that seems to --

A. Oh, I'm sorry.

Q. -- unfairly characterize --

A. That was a rhetorical question. I'm sorry. I was thinking

about -- the -- would I revise that statement? No. I would think that there was -- at -- back in 19 -- so -- well, by the time something gets published, you know, oftentimes there's like -- I mean, I think, you know, like about a six-month delay between the initial writing of this, so -- and then the literature, you know, published up to that point in time only takes us up to like 1997 maybe.

So up to that point, there wasn't a tremendous amount of information that allows you to make an estimate of the -- of DTC.

Q. Let's look at Exhibit No. 12 that you authored, which is the 2004 article from CNS Drugs, and what section was this published in?

A. This is published in the current opinion section.

Q. Okay. So this is --

A. And this was a solicited thing, so CNS Drugs said, Hey, look, here's somebody who's written about -- knows the literature of the impact of

direct-to-consumer marketing really, really well, and we're specifically interested in what would be the impact related to neuropsychopharmacologic substances, and let's have this person comment on -- on the basis of his expert knowledge of the literature on the potential impact related to those kinds of medications specifically.

Q. They wanted you to express your current opinion, right?

MR. JENNER: Objection.

A. They wanted me to express my -- the state of knowledge, okay, about the impact of pharmaceutical marketing, and then they asked me to make -- render opinions about the nature of that impact.

Q. (By Mr. Christian) Okay.

A. Professional opinions based on the cumulative evidence.

Q. Okay. Cumulative evidence up to that time of 2004, right?

A. Yeah.

Q. Okay.

A. Well, you know, as I

mentioned a minute ago, with -- given the delays in tasks of writing, publication -- you know, the things -- times it takes to get things to publication so, you know, you've got to --

Q. According to the best of your ability and available knowledge?

A. Yeah.

Q. Turn to Page 71 of Exhibit No. 12.

A. We're on 12 now?

Q. Yes.

A. Uh-huh.

Q. And if you look on the right-hand column and go down to the last full paragraph. Are you with me there?

A. Uh-huh.

Q. And you asked the same question that we're talking about in your report. Are there compelling data to suggest whether, on balance, DTC marketing leads to the right patients getting the right treatments at the right cost, or the wrong patients getting the wrong treatments at the wrong cost.

Q. And -- I'm trying to see -- and what you say on Page 23 of your report, Exhibit 4 -- do you have that?
A. Hold on a second. Page 23.
Q. You see the paragraph starting with "The Kravitz study"?
A. Uh-huh.
Q. You said it was a cleverly designed randomized control study that reveals the impact of this marketing strategy; is that correct?
A. Yes.
Q. Okay. And even though Kravitz undertook this cleverly designed randomized control study, he was -- the study could not determine the extent to which patient behavior is appropriately or inappropriately influenced by direct-to-consumer advertising; isn't that correct?
A. This study specifically couldn't.
Q. Okay.
A. But we can use the sum of available evidence on -- on prescriptions

dispensed, and physician prescribing behavior.
We can look at a host of other different studies to make our best professional judgment about the impact of direct-to-consumer marketing on patient behavior. So --
Q. Okay. So what happened with Kravitz is, he did this study to look at the impact of marketing strategy on a particular type of medication.
A. Well, again, so he looked at -- so what Kravitz did was, they --
Q. Antidepressant medication, right?
A. -- examined what happens when physicians in primary care clinical settings are presented with specific requests for drug therapy.
Some of those requests were, you know, just general requests, and some of the requests were requests for a specific drug based upon DTC, and some of the requests were just for help.
Q. Okay. And even though --

A. And they were role-played -- it was all -- you know, it --
Q. I know.
A. Yeah.
Q. He undertook the study, and he was unable to answer that question to the extent to which patient behavior is appropriately or inappropriately influenced by direct-to-consumer advertising?
A. The study wasn't designed to look at differential activation. And so to look at the extent to which differential activation actually occurs, we have to go out to other sources of available literature to render opinions about the impact.
Q. Doctor, I didn't think I was going to have to be fighting with you about what you've written in your report. If you look at Page 23 --
A. Uh-huh.
Q. -- you say that, Unfortunately -- of your report, right here.

A. Uh-huh.
Q. -- the extent to which patient behavior is appropriately or inappropriately influenced by direct-to-consumer advertising could not be determined from this study.
A. Uh-huh. That's what I just said to you.
Q. Yeah. Okay.
A. That's the exact same thing I just said to you.
Q. Now, you have not undertaken a study like Dr. Kravitz has done to look at whether or not you could see with respect to promotional activities of Wyeth whether or not it appropriately or inappropriately influenced patient behavior?
A. I have used other skills in my expertise to evaluate the extent of differential activation.
Q. But you have not undertaken a study like Dr. Kravitz did --
A. Well, I --
Q. -- with respect to hormone

therapy?
A. Huh?
Q. You --
A. I have not undertaken a randomized control trial, but a randomized control trial is only one form of science.
Q. Okay. And you haven't done that form of science, correct?
A. I have not done specifically that form of science.. It's --
Q. And subsequent --
A. But it's not necessarily the way you would get at answering questions of differential activation, so . . .
MR. JENNER: Counsel, we -- whenever you're ready for a break, whenever you're at a good stopping point.
MR. CHRISTIAN: I'm almost there.
MR. JENNER: Okay.
Q. (By Mr. Christian) Going

back to Exhibit 11, 2005.
A. Okay. I'm ready. What page did you turn to?
Q. Turn to 2032. What you say in 2005, starting right there, that -- you ask the question, Do the benefits of direct-to-consumer advertising outweigh the danger that consumers will demand and use medicines inappropriately? On balance, you say, the answer appears equivocal, and it awaits further research, correct?
A. Uh-huh.
Q. Is that a yes?
A. I'm sorry. Yes.
Q. Okay. And there's been --
A. But again --
Q. -- no research on this issue that's come out since April of 2005?
A. This refers specifically to -- on balance it refers to the general impact of direct-to-consumer marketing on our healthcare system.
So on balance, we don't

know if the answer is, in sum, it's good for the populations health, or, in sum, if it's poor -- if it negatively impacts.
In specific circumstances, we can use the rules that I've outlined here in my report before to evaluate specific circumstances, such as hormone supplementation, to evaluate whether or not on balance it's healthful or harmful.
So that's the -- that's the answer. But looking at -- if you're trying to get a big picture perspective, we really don't have -- as I said in the -- in the -- we don't have a -- we really lack a comprehensive framework that organizes these diverse health outcomes, behavioral, economic, health policy, business models that can be applied to DTC marketing research, so we don't have that big picture tool yet.
MR. CHRISTIAN: Objection. Nonresponsive.
Q. (By Mr. Christian) My question is, in April 2005, when you say the answer appears equivocal and awaits

further research, has there been any research that you can point to since April of 2005 which would help answer the question, do the benefits of direct-to-consumer advertising outweigh the danger that consumers will demand and use medicines inappropriately?
A. I stay really current on this research, obviously, because it's -- you know, it's relevant to all of the academic work that I do on it, and the answer is that there is not further research that summarizes in gen- -- in a broad sense the impact of direct-to-consumer marketing on health -- on the health of the American people.
But it doesn't preclude us looking at specific cases like hormone supplementation and the impact of Wyeth's promotional activities.
Q. Has there been further research which has looked and been published about Wyeth's specific promotional materials since April of 2005?

A. Not that I'm aware of, but there -- not -- not peer-reviewed publications of that.

MR. CHRISTIAN: All right. Let's take a break.

THE VIDEOGRAPHER: Going off record. The time is 11:48.

(Recess.)

THE VIDEOGRAPHER: We are back on record. The time is 11:59.

Q. (By Mr. Christian) Dr. Hollon, in critiquing Wyeth's promotional efforts with respect to hormone therapy, you characterized that promotional effort throughout your report, which is Exhibit 4, that it was -- included overzealous marketing schemes. Is that --

A. Let me say -- I would say -- if the question was phrased in evaluating Wyeth's marketing, then I would say that -- that -- one moment. I would say specifically like comments from the 1992 brochure state --

Q. I am just asking you about what your opinions are.

A. Yes, sir. Yeah.

Q. I'm just --

A. My professional opinion is that, based on comments from 1992 on a representative brochure that implored patients, So please, when you begin Premarin, stay with it to get all the long-term benefits it has to offer. Take an active role. Doesn't lack -- don't let lack of estrogen rob you of a healthy productive future you deserve, is overzealous.

Q. And you also think the promotional campaign was overly aggressive, correct?

A. Can you --

Q. Well, I mean, do you have that opinion? I just --

A. Not specifically do I use that phrase.

Q. Is that your opinion?

A. Well, what's my opinion is in my report.

Q. Right. And so if it says that Wyeth's efforts at marketing was overly aggressive, then that's -- you'd agree with that?

MR. JENNER: Objection.

A. Well, we'd have to go and look and see what's -- if it's in my report.

Q. (By Mr. Christian) You can't answer that question without looking at your report, why you think Wyeth's promotion of hormone therapy was overly aggressive?

MR. JENNER: Objection.

A. I would like to see where in my report I phrased it exactly like that.

Q. (By Mr. Christian) So you can't answer that question, just sitting there?

MR. JENNER: Objection.

A. It's not a question of can or can't, I guess. I -- what I want to do is, I want to see it in the -- where I used that phrase specifically in the

context of my overall document.

Q. (By Mr. Christian) I understand you want to do that. I want to know if you can answer that question just the way it's phrased.

A. I guess I would --

MR. JENNER: Do your best to answer the question straight up.

A. Yeah, I would answer that -- that they -- you know, that it was aggressive in the sense that they utilized aggressive integrated marketing tactics that targeted physicians and patients together, such that physicians ultimately prescribed hormone supplementation in the face of patient requests.

Q. (By Mr. Christian) So do you agree it was overly aggressive? That's what your opinion is?

A. I think that that's safe to say it that way.

Q. You cite from a document the language about a crusade more than a

MR. JENNER: Let him finish his answer, please.

A. Again, I'm not a FDA expert, so when they lay down this initial -- when they send this initial letter, the extent to which that should subsequently influence, but the fact is that there were no studies done -- I can confidently tell you -- between 1991 and 2000, there were no studies done that documented that the hormone -- the Premarin family of hormone supplementation improved vitality in women.

Q. (By Mr. Christian) You've seen no correspondence between the FDA and Wyeth regarding the Lauren Hutton vitality campaign, correct?

MR. JENNER: Objection.

A. Not that I can recall.

Q. (By Mr. Christian) Okay. You next cite another letter, in 1991, from the FDA to Wyeth, correct, regarding the Seasons magazine?

A. Later -- are we talking

later in February 1991, the FDA --

Q. Right.

A. -- also took exceptions with respect to promotions of Season magazine.

Q. And do you know why Wyeth submitted the Seasons magazine to the FDA before it was put into use?

A. Again, you know, I've never worked for the FDA, so -- but my recollection was that they actually did, but I can't be certain of that.

Q. Okay. And did Wyeth make the changes requested by the FDA with respect to Seasons magazine?

A. I think I remember seeing a letter that, at that point in time, they acknowledged these changes, or they acknowledged this -- they acknowledged the FDA requests, and they subsequently made some changes, but disputed others, but again, I -- I can't recall specifically.

Q. And do you know whether or not the FDA then accepted those changes

and approved the Seasons magazine with those changes?

A. Well, at that point in time, I can't recall specifically, but it does lay out that they shouldn't be promoting -- I mean, the beauty of -- excuse me. The value of this initial FDA letter says that discussions about moodiness and cardiovascular prevention are -- are -- fall outside of FDA expectations.

And that what we do know then, from looking at Wyeth documents, is that in subsequent years the promotion of -- by Wyeth of cardiovascular benefits of the Premarin family of drugs continued unabated.

MR. CHRISTIAN: Objection. Nonresponsive.

Q. (By Mr. Christian) Out of all of these letters that you cite, six different letters from the FDA, do you have any idea whether or not Wyeth responded to those letters, and that any deficiencies seen by the FDA according to

their regulations were later corrected?

MR. JENNER: Objection.

A. I have some sense that Wyeth responded to these letters and often would make short-term changes, but then return to the unabated strategy of promoting cardiovascular benefits despite being admonished not to do so.

But again, not being a regulatory expert and not having worked within the FDA, I can't comment on the full scope of communication. My expertise lies more in the impact of marketing of prescription drugs and public health prevention and osteoporosis.

Q. (By Mr. Christian) Let's look at Page 35 of your report. And Footnote 179, you talk about a -- DDMAC responding to Wyeth's requests for a meeting to discuss lipid claims; is that correct?

A. The DDM -- excuse me. DDMAC noted that Wyeth had failed to address new information available, and

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could tell, they never followed through with those regulatory -- that regulatory effort because they were concerned that it would limit their ability to promote cardiovascular benefit.

It's clear then, subsequently, from the citizen petition on behalf of Wyeth, that they don't feel that restraint in submitting that petition.

Q. Do you know how many complaints to the FDA about competitor promotion of hormone therapy products that Wyeth made before the WHI study?

A. Well, I couldn't speak to exactly how many complaints they made about competitor therapy, but it -- you know, there's definitely evidence that they exhibited some level of restraint.

Q. Just based upon that one document that you've referred to?

A. That's some level of restraint.

Q. You don't know how many they sent to the FDA before WHI versus

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how many they've sent after the WHI, do you?

A. What I would say is that, while I'm unaware of how many exactly they have or they haven't set -- sent, it would really depend on the details of those actions for me to make any particular comment on their relevance, or how they influence the overall picture.

Q. Do you know what bio-identical hormone replacement therapy is?

A. I'm not an expert in alternative medicine therapies, and I know of them in the context as a practicing clinician.

Q. And so that is considered -- bio-identical replacement hormone therapy is considered an alternative therapy?

A. To the best of my understanding, it's considered an alternative therapy, although they have physiologic -- well, I guess most alternative therapies have physiologic actions. These ones are thought -- or believed to mimic more intensely

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physiology of -- of estrogens.

Q. Do you know whether the Food and Drug Administration has approved a safe and effective bio-identical hormone replacement?

A. I'm unaware of whether or not the Food and Drug Administration has approved a safe bio-identical. My suspicion, if I -- on the basis of my clinical expertise, I would presume that they have not.

Q. You would be correct.

So what allegations did Wyeth make in that complaint to the FDA about bio-identical hormone replacement?

A. Well, let's pull up the document.

Q. Okay.

A. I -- off the top of my head -- we could go over it. I think -- I think the bulk of them, if I remember correctly, were around cardiovascular concerns, but it was far-reaching.

It might have been -- the document might have been like 55 pages

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long or something like that. So without us pulling out the document and going through it, you know, I'm not speaking as confidently as I would like.

Q. Okay. Do you know whether or not compounding pharmacies that were selling and promoting bio-identical hormone replacement were following good manufacturing practices set forth by the FDA?

A. I can't comment.

Q. All right, sir. The -- you've referred to several advertisements relating to hormone therapy put out by Wyeth in your report; is that correct?

A. That's correct.

Q. Okay.

A. Several, I think, is a reasonable summary. More than several.

Q. And do you know which of those ads appeared to be, you know, finished ads that were actually run, or finished promotional pieces that were used?

A. I reviewed -- sometimes it

was hard to distinguish between what were finished and unfinished, but I have -- I did have a catalog or binder of ads that were taken, for example, as -- the example of direct-to-consumer marketing, a binder of ads taken directly out of print magazines, as well as reviewing television advertisements, as well as reviewing promotional material that direct -- was directed at healthcare providers.

Q. Ads that you're criticizing regarding Wyeth's promotional practices are referenced in Exhibit No. 4, your report, correct?

A. Which ones are you referring to specifically, or what page?

Q. Well, are -- is that what you did in writing your report, in giving your summary of your opinions in this case, and --

A. Is what what I did?

Q. Did you identify the Wyeth ads that you're criticizing?

A. Well, I think the bulk of

my evaluation and summary opinion about Wyeth comes from the overarching intentions of their marketing campaign that were revealed subsequently in certain advertisements.

And so I -- when I came across advertisements that were consistent with the overarching intention to make sure that all menopausal women, regardless of their chance of fracture, hip fracture, ended up on a carcinogenic substance, I -- when I found these advertisements that reflected that policy, exaggerating or -- let me rephrase that -- misleading women about their chance of dying from hip fracture, I would hold on -- you know, I would use those as an advertisement that represents the policy delineated in marketing documents that Wyeth produced.

Q. Okay. Since it would probably take you a while to pull all of those out of your report, I've done that for you ahead of time.

A. Are you done with this for

now?

Q. Yes.

(Exhibit No. 25 marked for identification.)

Q. (By Mr. Christian) And I'm marking as Exhibit No. 25 the advertisements referenced in your report that appear to be final ads that may have been run in the United States or elsewhere.

Would that seem to --

A. Yes.

Q. -- be a fair presentation of those ads, as far as --

A. I think that "seem" is a -- would be an accurate reflection. Whether it represents the entire -- all of the advertisements, I can't say off the top of -- or off my -- off the cuff.

Q. And did you take these advertisements in Exhibit 25 and do a systematic review of them to determine if they were in compliance with the Food and Drug Administration regulations?

A. You'll need to explain to me what you mean by "systematic review."

Systematic review has a very specific meaning, at least in a -- in a clinical context --

Q. Okay.

A. -- when we talk about -- primarily relating to evidence-based medicine and the techniques used to evaluate medical literature.

We wouldn't typically do systematic reviews on advertisements, so I think that we have a bit of a miscommunication around --

Q. Did you do any kind of review of the ads in Exhibit 25 to determine if they comply with Food and Drug Administration regulations regarding direct-to-consumer advertising?

A. I am familiar with the regulations and reasonable standards of care based on my expertise in promotion of pharmaceutical agents to patient and physicians, and I evaluated these advertisements on the basis of that expertise.

Q. I understand that. My

misleading statements. And so I'm not going to say for the record that there's absolutely no untrue statements in this stack.

Q. (By Mr. Christian) That's fine. That's all I'm asking.

Now, you took your background and experience and reviewed these ads in Exhibit No. 25, and read through them, right?

A. Correct.

Q. Okay. Do you know whether or not the Food and Drug Administration reviewed the ads in Exhibit 25 to see if they were false and misleading or not?

MR. JENNER: Objection.

A. I can't speak for the FDA.

Q. (By Mr. Christian) Okay. Do you know which ads in Exhibit 25 that any of the plaintiffs in this case saw?

MR. JENNER: Objection.

A. I know that there are statistics that Wyeth speaks to about the frequency or the anticipated frequency with which the population of women in

this country would see certain campaigns. They're -- studied this issue intensively, and so they would say there -- we could go through here and figure it out. But just off the top of my head, they would say, Well, I can promise you that six -- you know, the average woman in the country will see this advertisement six times in the next three months.

Q. (By Mr. Christian) That doesn't mean that every woman in the country saw the ad in the next six months, correct?

A. But on a probabilistic basis, when we're talking about several million women taking this -- you know, what eventually proved to be a carcinogenic -- carcinogenic substance, there is a probability beyond a reasonable doubt that women were influenced or healthcare providers -- we're talking about promotion in general -- were influenced by these advertisements.

Q. Identify for the jury the ads in Exhibit 25 that Linda Reeves saw.

MR. JENNER: Objection.

A. I haven't spoken with Ms. Reeves.

Q. (By Mr. Christian) Can you identify for the jury the ads in Exhibit 25 that Helene Rush saw?

MR. JENNER: Objection.

A. Once again, I can't -- I've never spoken with Ms. Reeves, although I can say that, on a more probable than not basis, there -- given the extent of the marketing campaign and the intensity of the promotional efforts by Wyeth, that the women and healthcare providers in this country were unduly influenced by a campaign that sought to make sure that all women, all menopausal women, were placed on hormone supplementation.

Q. (By Mr. Christian) Doctor, is it your testimony in front of the jury in this case that you can't tell the jury a single advertisement in Exhibit No. 25 that any of the plaintiffs in this case

saw? Can you say that?

MR. JENNER: Objection.

A. All I can say is that, on a more probable than not basis, this marketing campaign, of which there are some representative advertisements, but this doesn't reflect the world of possible advertisements, on a more probable than not basis, that these advertisements impacted the decisions that patients and providers made together.

Q. (By Mr. Christian) You say it impacted the plaintiffs in this case?

MR. JENNER: Objection.

A. It impacted the decision that millions of patients and providers in this country made together. Now, whether or not those people are amongst the -- you know, whether that million or two million --

Q. (By Mr. Christian) You don't know?

A. -- is -- specifically includes the plaintiffs in this case, I'm

not sure anybody could speak to. Because the other concern here is that a lot of times people can't specifically identify the sources of -- predominant sources of the -- of influence, and particularly for healthcare providers, there's a lot of -- of -- of -- of -- of sources of information out there that were cultivated by Wyeth that doesn't clearly identify that the source of the promotional information was from Wyeth.

Q. Just as you say a plaintiff may not be able to specifically identify what promotional items persuaded them, the same goes for you; you can't say which promotional item persuaded any plaintiff or not persuaded any plaintiff in this case, correct?

MR. JENNER: Objection.

A. I'm sorry. Say that again.

Q. (By Mr. Christian) You were saying that a plaintiff may not be able to specifically identify promotional piece that they saw. Neither can you. That applies to you, too. You cannot

identify a specific promotional piece that any of the plaintiffs in this case saw?

A. What I can say, though, beyond a reasonable doubt, is that the cumulative effects of the promotional campaign by Wyeth unequivocally influenced decisions about who was placed on Prempro and for how long.

And I mean, the flip side of the way to look at this -- the flip side of the way to look at this is to say, Let's just take the entire promotional campaign away and ask ourselves to pause -- to think for a moment, would there have been nearly one billion prescriptions from the Premarin family written up to 2001?

And I think we sit -- personally -- I mean, excuse me, professionally, beyond a reasonable doubt -- professionally, beyond a reasonable doubt, those pre- -- one billion prescriptions would not have been written.

MR. CHRISTIAN: Objection. Nonresponsive.

Q. (By Mr. Christian) When I asked you a question about what you can't say, you answered it -- you go on with what you can say. I know what you can say.

Can you answer my question about that you can't say which particular ad any of the plaintiffs in this case saw, a particular ad?

MR. JENNER: Objection. Asked and answered.

A. I'm trying to give you the best answer that I possibly can.

Q. (By Mr. Christian) Okay. And the best answer might be that you can't say that.

MR. JENNER: Objection. Asked and answered.

A. No, the best answer that I can give to that is that what I can do, based on my expertise in pharmaceutical promotion, my understanding of population prevention and osteoporosis is that the

sum of this campaign under duly influenced prescribing decisions in this country and led to millions of women, on a more probable not -- than not basis, some of which, you know, on a -- on just a chance basis, were likely to include the plaintiffs and their prescribing providers.

Q. (By Mr. Christian) I understand that you're saying it's more likely than not they would have saw these, but you cannot say definitely --

A. I can say more likely than not.

Q. I understand that. But you can't identify definitely an ad that they saw?

A. With 100 percent assuredness?

Q. Right. Right.

A. I can't say that for 100 percent assuredness.

Q. Okay. Thank you.

The first ad in Exhibit 25, what magazine did this run in?

A. I'm uncertain.
Q. Do you know what time period this ad ran?
A. Do you know where it's referenced in my report? We could probably -- we could work backwards that way.
Q. Exhibit 202.
A. So that's Footnote 202?
Q. Right.
A. So representative advertisements from 19 -- this is 1970, although -- so I would guess that this is from on or around the 1970s.
Q. Do you know when in 1970?
A. I don't know when.
Q. Do you know what journal it ran in?
A. No, I can't speak to that specifically. I'd have to go back and look at all my notes about how I identify that this came from on or around the 1970s, so I can't recall specifically how I was able to.
A lot of the times the

documents didn't have specific dates, so there were a variety of ways that I would either look at reference lists to try and get an accurate representation of the approximate date because I didn't want to get it out of sequence to misrepresent the nature of the campaign.
Q. Okay. I'm going to sub-mark these 25 -- Exhibit 25 into letters so that the record will be clear. The first one we were just talking about is 25-A.
A. Uh-huh.
Q. I'll just go ahead and mark all of these.
A. Okay.
Q. Back to 25-A real quickly. Which plaintiff in this case, or which prescribing physician in this case saw Exhibit 25-A?
MR. JENNER: Objection.
A. Again, I would wonder whether the prescribing physician in the case would even be able, or would even willingly identify an advertisement that

had influence on their practice.
Q. (By Mr. Christian) So the answer is, you can't identify one of the prescribing physicians in this case that saw Exhibit 25-A, can you?
MR. JENNER: Objection. Asked and answered.
A. Ask me again.
Q. (By Mr. Christian) So your answer is that you can't identify a prescribing physician in this case that saw Exhibit 25-A?
A. No. But again, given the extent of the campaign, on a more probable than not basis, there were lots of physicians that did see these advertisements.
MR. CHRISTIAN: Objection. Nonresponsive, everything starting with the word "but."
Q. (By Mr. Christian) Okay. Let's look at Exhibit 25-B. Do you know what magazine or journal Exhibit 25-B ran in?
A. No. I can't tell you that.

Q. Okay. Do you know whether this ad ever ran at all?
A. This looks unfamiliar to me. Do you know where it's cited in the report? I'd like to see it in a context.
Q. It's at Footnote 205.
A. Oh, undated. 205. Well, there -- this one makes a statement about -- I'm uncertain whether this advertisement ever ran at all. I use this mostly to illustrate not, per se, advertisements, but that Wyeth was advancing a concept of a menopause -- of menopause as a disease by equating it with insulin deficiency disease of Type I diabetes, which is horribly erroneous to make that -- to make that equation.
And they were doing this -- they were trying to set up this paradigm that they intended to utilize in all of their marketing over the ensuing decades around the idea that this estrogen deficiency -- that there was this estrogen deficiency state disease.
MR. CHRISTIAN: Objection.

Nonresponsive to everything after "I'm not sure this is an ad that ever even ran."

Q. (By Mr. Christian) I know you haven't ever given a deposition before; is that right? We established that?

A. We established that.

Q. Okay. Did anyone give you any instructions about how to answer questions for a deposition?

MR. JENNER: Objection.

A. Not specifically.

Q. (By Mr. Christian) Did anyone tell you to not answer the questions that are being asked?

MR. JENNER: Objection.

A. No. In fact, I was actually told that the purpose of the deposition was for me to -- for -- for Counsel to ask questions, and for me to answer the questions.

Q. (By Mr. Christian) Okay. Did you review Pages 1 to 5, and any pages that came after 6 in Exhibit 25-B?

Do you see that's marked Page 6 down there at the bottom left-hand corner?

A. Do you have those pages available for me to review? Without looking at them, I can't recall if I saw them.

Q. I don't have them with me, but this is all that's cited in your report, so I don't know if you just picked this page out or --

A. If it was buried within the -- if it was buried within a series of documents, I probably saw the ones before and after.

Q. Okay. All right. Let's look at 25-C. I guess you can tell us where this ad ran?

A. Contemporary OB/GYN.

Q. And do you know whether any prescribing physicians in this case saw Exhibit 25-C?

MR. JENNER: Objection.

A. I'd answer that by saying that I don't know specifically if any prescribing physicians, but on a more

likely than not basis, it was probable that some physicians that were involved in the -- in the litigation would have seen these ads, given -- or some version of these ads.

I don't know about this specific ad, but would have seen some -- or would have been exposed to the marketing influence of Wyeth's promotiona materials.

Q. (By Mr. Christian) Exhibit 25-D. Do you know where this promotional piece ran?

A. I don't know where this promotional piece ran.

Q. Do you know what time period this piece was used?

A. Can you give me the point at which it occurs in my report?

MR. JENNER: 207.

A. I would estimate in the -- in the mid-1970s.

Q. (By Mr. Christian) And you cannot say whether or not any prescriber or plaintiff in this case actually saw

Exhibit 25-D, can you?

MR. JENNER: Objection.

A. Not this specific advertisement.

Q. (By Mr. Christian) Exhibit 25-E is Footnote 220 in your report?

A. I mean, my report is organized chronologically, so with respect to the dates of all of these that they were either developed and/or ran, it's -- basically the approximate date could be determined from the report.

Q. Okay. You say that this ran in 1987, in your report; is that correct?

A. It's copyrighted 1987 Ayerst Laboratories.

Q. Okay. But you don't know if it ran in 1987 or some other time, do you?

A. Well, I'm -- I can't speak specifically to at what point the advertisement was used.

Q. Okay. And can you say

whether any prescribing physician in this case, or any plaintiff in this case specifically saw Exhibit 25-E?

MR. JENNER: Objection.

A. We have now this growing body of advertisements that we're going through, and on a more probable than not basis, some of the people involved probably saw something along these lines, but I can't say specifically about that one there.

MR. CHRISTIAN: Okay. Objection. Nonresponsive, except for "can't say specifically except [sic] for that one there."

Q. (By Mr. Christian) Exhibit 25-F, this is Footnote 234 in your report.

Do you know where Exhibit 25-F was used?

A. Promotion strategies that prey on patients' fears is inappropriate marketing and violates the standard of care because it lacks proper balance.

Q. Okay. I'm not asking you to read your report.

A. I'm sorry. I'm just trying to -- that helps me --

Q. I know, but you don't need to read your report out loud. You can just tell me where this ad ran.

A. Okay. I'm sorry. End of the decade, concludes that a physician can now -- I mean, it's an interesting misleading statement, but I can't tell you where it ran at all.

Q. Okay. Or what time period?

A. Well, again, using -- as I've elaborated before, I was able, to the best of my abilities, either by using a copyright date or triangulating against the hard drive and looking if there are -- I don't know if there are page -- you know, if this is the complete document, it would -- based on the report, it's likely to have been produced and/or used at the end of the 1980s.

Q. Okay. And you cannot say, with respect to any specific prescribing physician in this case or any plaintiff, whether they saw Exhibit 25-F?

MR. JENNER: Objection.

A. Well, not this specific advertisement, again, but they were likely to have been influenced by the now accumulating stack of advertisements that are sitting in front of me.

MR. CHRISTIAN: Objection. Nonresponsive, starting with the word "but."

Q. (By Mr. Christian) Looking at Exhibit 25-G, which is Footnote 236 in your report, you identify the date as April 1990 for this piece, correct?

A. The effort to scare women about the gravity of osteoporosis? That one?

Q. You identify Exhibit 25-G as coming from April 1990, correct?

A. Right. I just want to make sure we're talking about the one that I believe represents an effort to scare women about the gravity of osteoporosis?

MR. CHRISTIAN: Objection. Nonresponsive.

MR. JENNER: He's asking a

question, which one you're talking about.

Q. (By Mr. Christian) I've referenced Footnote 236, right?

A. 236.

Q. Okay.

A. Yes.

Q. Okay. And do you know what journal or magazine Exhibit 25-G ran in?

A. It's not stated on this advertisement here.

Q. And you don't know, correct?

A. And for that reason, I don't know.

Q. Okay. And you cannot state whether any doctor -- prescribing doctor in this case or any plaintiff saw Exhibit 25-G, can you?

MR. JENNER: Objection.

A. My answers to that would be the same answers as before, which is not specifically.

Q. (By Mr. Christian) Okay. Just to shortcut it then, can I get that

there, and that's not the question I asked you.
A. Uh-huh.
Q. Okay.
A. So --
Q. Without the word "randomized," is that statement accurate?
MR. JENNER: Objection.
A. I'd say the statement is misleading.
Q. (By Mr. Christian) Under "Bone," "Decades of research have proven that estrogen loss decreases bone mineral density and increases the risk of fractures from osteoporosis."
Is that accurate?
A. Yes.
Q. Under "Colon: Ongoing epidemiological research continues to explore the risk of colon cancer among women after menopause."
Is that accurate?
A. Yes.
Q. All right, Doctor.
A. Are we done with this one?

Q. Yeah.
MR. CHRISTIAN: Why don't we take a break here. I'm at kind of a transition point.
THE VIDEOGRAPHER: Going off record. The time is 2:56.
(Recess.)
THE VIDEOGRAPHER: We are back on record. The time is 3:10.
Q. (By Mr. Christian) Okay, Dr. Hollon, are you ready to proceed with your deposition?
A. Yes.
Q. Okay. You talk about, in your report, some document that you reviewed from a company called DesignWrite.
Do you recall that?
A. Yes.
Q. And in it, you talk about something called ghostwriting, correct?
A. Can you take me to the page that you're referring to, please?
Q. 62.
A. Is there a specific

paragraph that you'd like me to look at?
Q. You can look at whatever you need to.
A. This one, In short, DesignWrite took over and then subsequently expanded dramatically the full reach of Wyeth's promotional efforts. This would include activities that most medical -- that most people in the medical community deemed improper such unrevealed conflicts of interest and the deceptive activity of ghostwriting.
MR. CHRISTIAN: Objection. Nonresponsive.
Q. (By Mr. Christian) What you say on Page 62, that, Ghost authorship exists when someone, such as an employee of DesignWrite working on behalf of Wyeth-Ayerst, has made, one, substantial contributions to writing a manuscript, and this role is not mentioned in the manuscript itself, correct?
A. Correct.
Q. Can you identify a

published medical or scientific article where a DesignWrite employee made a substantial contribution to writing a manuscript and that role was not mentioned in the manuscript?
A. Unfortunately, I didn't have time to go and get this manuscript from the -- from the library, so I have the abstract with the authors listed here.
This is the one that I actually -- I was curious if it actually -- before I ever did this, I was curious if the -- what appeared to be comprehensive plans for ghostwriting ever led them to have actually success.
This is a really disconcerting topic for those of us who rely on the medical literature to provide us with what we hope at their core are responsible pieces of medical science. And by "responsible," I mean that the science is well done, that all the people --
Q. Doctor, I only have a

call it misleading, but it, beyond a reasonable doubt, is deceptive.

And those kind of activities really, in my mind, subsequently undermine our -- our confidence in the medical literature as a whole that would surround the hormone supplementation.

Q. Is there anything inaccurate in the article that's referenced in Exhibit No. 28?

A. I suppose the inaccuracy is that there is no author listed -- no -- no employee of DesignWrite listed in the authorship.

Q. Is there any substance, scientific substance, in the article, Exhibit No. 28, that is inaccurate?

A. I'm not a sex hormone-binding globulin expert, and so I wouldn't feel that that would be within my abilities to comment on.

Q. Were you able to identify, in your opinion, any other published medical or scientific article where a

DesignWrite employee made a substantial contribution to writing a manuscript and their role was not mentioned?

A. There's a host of -- I didn't have time to -- this would have been a very intensive process. I didn't have time to go and put together the long list of anticipated publications that DesignWrite was crafting.

There is an interesting piece here where they talk about having secured 16 authors for 20 of these publications, but I don't have the specific ones that, beyond a reasonable doubt, appear to be ghostwritten, in front of me today.

Q. Okay. Now then, you talk about DesignWrite assisting Wyeth in controlling and influencing information regarding hormone therapy, correct?

A. What page is that specifically, please?

Q. I just have that from my notes without a page. Do you -- does that sound --

A. I want to find it because I want to make sure that the way that you're quoting me is what I've written. If you want to -- I can keep looking. It sounds approximately correct.

Q. Okay. Then you go on to say -- and I'm sorry; I don't have the page cite for this -- that Wyeth has created or managed almost all sources of information about Premarin, Prempro available to doctors and women.

A. Now we really need to find the page.

Q. Okay.

A. So I can read that in the context of the larger one. I kind of know approximately where it -- no, that's too far.

There's a paragraph where Jeff Solomon talks about how Wyeth recog- -- According to Jeff Solomon -- Page 64. According to Jeff Solomon of Wyeth marketing, one of the rationales for the publication program was the recognition of high clinician reliance on

medical articles or journal articles -- journal articles for credible product information. DesignWrite thanked Jeff for awarding it the publication plan in support of the brand and in defense of raloxifene competitive threat.

And then the next paragraph, DesignWrite assisted Wyeth in controlling and influencing the published scientific information about hormone supplementation that most clinicians ultimately relied on to make their best possible decisions. Controlling this information such that it was favorable to the Premarin family, and menopausal hormone supplementation in general, would prime healthcare providers to be receptive to the demand generated by patients influenced by the company's DTC marketing schemes.

MR. CHRISTIAN: Objection. Nonresponsive.

Q. (By Mr. Christian) Doctor, if you want to read through your report, can you do that on your own time, and we can have the record going after the end

of this deposition if you want to go past the end of your seven hours and read your report, you're welcome to do that?
MR. JENNER: Objection.
A. We're trying to find, though, where the stuff is so I can comment --
Q. (By Mr. Christian) Reading all that doesn't help us much, I don't think.
Let's look at the bottom of Page 64. It says, "DesignWrite assisted Wyeth-Ayerst in controlling and influencing the published scientific information about hormone supplementation that most clinicians ultimately relied on to make their possible decisions."
A. Uh-huh.
Q. Okay. And the only thing that we've been able to identify that's published scientific information is the Exhibit No. 28, correct?
MR. JENNER: Objection.
A. That's all that we've had time to identify to this date, but it

doesn't mean that there's not -- I mean, DesignWrite's plan was for 20 publications per year. I mean, they had -- most scientists -- good scientists produce one or two publications a year.
You're talking about 20 publications a year, and there's reasonable evidence that the whole process that was working to produce all of this literature around some really interesting or notable, noteworthy topics, was moving forward.
Q. (By Mr. Christian) Do you know how many textbooks there are that discuss scientific information about hormone therapy?
A. Lots.
Q. Okay. Do you agree that there's been thousands of articles in the medical literature on menopause and hormone therapy?
A. I can't quantify exactly how many there have been.
Q. Would you dispute that there's been thousands?

MR. JENNER: Objection.
A. No.
Q. (By Mr. Christian) Okay. And out of those thousands, how many do you believe Wyeth had control over?
MR. JENNER: Objection.
A. I can't quantify that specifically.
Q. (By Mr. Christian) Did you make a comprehensive analysis of the hormone therapy literature to determine how many, if any, articles on hormone therapy was funded by Wyeth?
A. Well, you know, this was a piece of the overall marketing plan that influenced providers and patients together.
The -- it was an important part of the marketing scheme that Wyeth continued to invest in. It's reasonable to suppose that they continued to invest in it because it was effective.
Q. But as you said, you haven't done that yet, go look to see whether or not other published articles

that meet that definition have been published, correct?
A. I have not looked specifically in PubMed. It was disconcerting enough to find that there was this effort out there to control and influence medical literature in a deceptive fashion.
MR. CHRISTIAN: Objection. Nonresponsive, to the second part of the question -- answer.
Q. (By Mr. Christian) Do you attend continuing medical education seminars?
A. I've put on -- I've participated in presenting at continuing medication -- continuing medical education seminars. I've attended national meetings that include the Society for General Internal Medicine.
Q. And do you know whether or not any pharmaceutical companies have sponsored all or part of these CMEs that you've gone to?
A. These are ones that I've

primarily to inform of the -- you know, the risk of fracture and mortality risk, that first one.

I have confidence and expertise in population prevention, and would tend to rely on that developed expertise about making assessments about strategies for population prevention, perhaps even more than I would rely on the United States -- on the technology of office assessment. I'd be interested in reviewing it again in more detail.

Q. Okay. As you sit here today, you don't plan on doing any additional work for trial in this case?

MR. JENNER: Objection.

A. I have no idea one way or another.

Q. (By Mr. Christian) Okay. Do you know what it means for a company to give an unrestricted educational grant to a medical education company?

A. Yes.

Q. Okay. If you look at Page 83 of your report, you talked

about -- and actually, this is, I think, listed several times throughout your report, this statement about Wyeth manufacturing clinical data.

A. Oh, yeah. Let me -- hold on a second. Let's see. I need -- I hope these are -- yes, I -- go ahead.

Q. Okay. Could you identify what data that you say Wyeth manufactured?

A. Well, by "manufacture," I mean that they set out to -- and delineated their intent to find and generate evidence that would be favorable to the Premarin family, and Prempro in particular. And so there are a number of examples about their efforts to -- to generate this data.

The footnote that I'm referring to here is when they long -- they developed these long-term tactics, including funding studies to demonstrate positive effects on sexuality, quality of life, and acute cognitive functioning, and they go on here to say, in an

underlined document, This acute cognitive symptoms is not well defined or articulated in medical literature. We must define it. Develop quick proof studies, and determine if there is potential for labeling or additional claim.

So that to me is -- is this strategy that -- this speaks to the overall strategy of -- of -- of manufacturing data. That's what I'm referring to.

Q. And the document you just referred to, is that one of the footnotes in your report?

A. Yeah. This is footnoted, right.

Q. Where at?

A. It's Footnote 408, and these are HRT Summit: Strategic Implications, Medical/Marketing Sub-team, a bunch of objective strategies.

Increase the awareness of early menopausal symptoms and expand the definition of menopause symptoms. So

here their goal is to expand the definition of menopause symptoms, so they then come up with this strategy in which they define what the condition is, and then they're -- with the goal of developing quick proof studies.

They actually rate their probability of success for a short, quick study as medium to high, and that the potential impact for those studies for indication labeling claim would be high.

Q. So where would I go to look at the data that you claimed Wyeth manufactured?

A. Well, this is just -- this is an effort on their part that's representative of, I think, you know, more comprehensive efforts. Their influence with -- through DesignWrite, I think would be another potential example of these -- this idea that you could create the necessary data.

Q. So you're unable to identify specific data that Wyeth manufactured, in your opinion?

MR. JENNER: Objection.
A. At the moment I'm not going to be able to give you a specific study that says, Well, this study was a study manufactured. The scope of their influence and their efforts was huge, as we -- as is revealed by all of this here, and so certainly their intent to do so is laid out in all of these different studies. And I believe that they, given the money that they spent on doing this, met with success.
MR. CHRISTIAN: Objection. Nonresponsive, everything after the word -- the first "the."
Q. (By Mr. Christian) You also say in your summary of opinions that Wyeth purchased professional opinions. Can you tell --
A. Hold on a second.
Q. Okay. Look at Page 3 of your report.
A. Yes.
Q. Okay?
A. Okay.

Q. You have a little list there of things that -- we just talked about manufacturing data. The next thing you have there is purchasing professional opinions; is that correct?
A. Yes.
Q. Tell me what professional's opinion was purchased in -- that you're referring to in this case?
A. Well, there are a number of different examples, but I think that people like Charles Hammond had developed ideas that included that hormone therapy would be used to prevent cardiovascular disease, that were subsequently put into the Duke monograph, and received money for development of the Duke monograph from Wyeth. So that to me is a purchased professional opinion.
Q. So your opinion is that Wyeth purchased the professional opinion of Dr. Charles Hammond, that was reflected within the Duke monograph?
MR. JENNER: Objection.
A. Can you say that again?

Q. (By Mr. Christian) It's your opinion that Wyeth purchased the professional opinions of Dr. Charles Hammond, which was reflected in the Duke monograph?
A. Correct.
Q. Okay. How much did Wyeth pay Dr. Hammond, in your opinion, to purchase this opinion?
A. I don't know specifically that information about the quantity of money that was paid for the Duke monograph, although it's -- Wyeth is -- gives -- there's an unrestricted -- there's a little thing on -- you know, this is -- we're giving money -- Wyeth is giving money to support the development of this.
Q. And that has been recognized by the FDA and others -- companies -- pharmaceutical companies giving unrestricted grant for medical education as very valuable?
MR. JENNER: Objection.
A. As very valuable. I'm not

sure if -- I won't speak on behalf of the FDA or other people about the value that they associate with it.
Q. (By Mr. Christian) So what -- what can I look at that supports your opinion that Dr. Charles Hammond's professional opinions were purchased by Wyeth?
A. The Duke monograph.
Q. Okay. That's your only evidence?
A. That's the one that I can pull off the top of my head at the moment. I think that there are other examples within the report that you're free to look at.
Q. Is there any other professional opinions that you believe Wyeth purchased?
A. There was one, I think, in my report on -- by Leon Speroff on the -- it would take me a -- I think a substantial time to find it within here. Let's see if I have footnotes related to that. No, I don't. About breast cancer